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Prenatal alcohol consumption: Exploring prevalence and the impact of an educational intervention

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Dedication

In loving memory of Therese Keating.

*

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Throughout the past few years, I've received a helping hand from many, and for that I am most grateful. First and foremost, I would like to express my sincerest thanks to the many women across the UK who kindly offered up their time to take part in this study, without whom this study would not have been possible.

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Thesis overview & structure

This thesis portfolio is comprised of two separate chapters: the first, a systematic literature review and the second, an empirical research project. The aim of the systematic review was to explore the prevalence of prenatal alcohol exposure as assessing using meconium biomarkers in general maternity populations. The focus of the empirical study was to explore prenatal alcohol use in the UK and the impact of an educational intervention on women's knowledge and attitudes, using a quantitative approach.

Both sections adhere to submission guidelines for the *BMC Pregnancy and Childbirth* Journal. Additional information for the systematic review and empirical study is presented within the references and appendix section of each chapter, which immediately follows the main text.

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Thesis Abstract

Background

Alcohol is a well-known teratogen and its consumption during pregnancy is a growing public health concern across the globe. Prevalence rates of prenatal alcohol use remain high, despite international guidelines recommending abstinence. This has significant consequences as it is a direct cause of foetal alcohol spectrum disorder, which is known to have widespread adverse effects on the individual, their families and wider society. Ascertaining the true extent of prenatal alcohol use remains a major challenge however as obtaining this information can be challenging.

Objectives

The purpose of the systematic review was to assess the international prevalence of prenatal alcohol exposure as obtained using meconium biomarkers in general maternity populations. The purpose of the empirical study was to explore the prevalence of prenatal alcohol use by self-report of women in the UK, and the impact of an educational intervention on attitudes and knowledge towards drinking during pregnancy.

Methodology

The systematic review was completed on studies reporting the prevalence of prenatal alcohol exposure as determined by meconium biomarker testing, and their methodological quality was appraised. A national anonymous online study was conducted for the empirical study. This comprised of an educational intervention and questionnaire measures assessing prevalence of self-report prenatal alcohol use, attitudes and knowledge.

Results

Findings from the systematic review demonstrated that prevalence rates of prenatal alcohol exposure assessed using meconium biomarkers varied from 2.4% to 44%. Studies were found to be of moderate quality, although varied greatly with respect to their sociodemographic and methodological characteristics. Findings from the empirical study demonstrated high rates of binge drinking prior to pregnancy (82%), which decreased significantly following recognition of pregnancy (0.2%). The educational intervention was found to have a significant impact on attitudes and knowledge ($z = -9.67$, $p < .001$ $r = 0.29$).

Conclusion

Results of the systematic review support the utility of meconium as a promising objective tool for the detection of prenatal alcohol exposure but recommends use with caution and adherence to stringent methodological protocols. Further research is warranted on its utility in clinical practice. Results of the empirical study support the use of educational interventions in improving women's knowledge of risks and increasing negative attitudes towards prenatal alcohol use. Recommendations for implementation of such interventions at community and clinical levels to reduce prenatal alcohol use and subsequent risks of foetal alcohol spectrum disorder are made.

Lay summary

Background

Drinking alcohol during pregnancy can cause long-term harm to the baby and, can lead to a range of deficits known as Foetal Alcohol Spectrum Disorder (FASD). The message from international health bodies such as the World Health Organisation and the UK's Chief Medical Officers is that the safest approach for pregnant women is to not drink alcohol at all. This guidance has changed overtime however and there has been conflicting advice as to whether or not small amounts of alcohol during pregnancy are harmful. This has led to different attitudes and beliefs amongst the general public healthcare professionals and despite the known risks, drinking during pregnancy remains a significant and growing public health concern across the globe today.

It is difficult to get a clear picture on how prevalent alcohol consumption during pregnancy is in society, and there has been different ways used to assess this in order for the baby and its mother to best be supported. One way to detect alcohol use in pregnancy is by analysing the first stool a baby passes after birth, which is known as the meconium. Alcohol and drugs consumed in the second and third trimesters of pregnancy are metabolised in the foetus and stored in this meconium. Meconium can be collected after birth and tested in a lab to indicate if the baby was exposed to alcohol. Positive meconium tests indicate heavier levels of drinking in the later stages of pregnancy. A second way to obtain information on alcohol use during pregnancy is through self-report. This is when women are asked about their alcohol intake by their healthcare professional, and can be done through discussion or by using questionnaires. Gathering this information is crucial for detecting babies who might be at risk of FASD, and mothers at risk of alcohol-related harm, as without it babies often go unsupported, undiagnosed, and the right treatment cannot be given.

Preventing and reducing alcohol use in pregnancy is crucial, and this is a major focus of public health interventions such as media campaigns and education interventions. These help to educate the general public of the risks associated with drinking in pregnancy.

Objectives

This thesis is made up of two chapters; the first is a systematic review and the second is a research study. The aim of the systematic review was to investigate all of the studies carried

out between 1990 and January 2021 which reported the prevalence of alcohol exposure during pregnancy by using meconium testing. It summarises results from 12 studies which included women who gave birth in general maternity settings. The purpose was to find out whether the research can indicate how common alcohol use in pregnancy is by using these tests. It also looked at the quality of the studies done and aimed to help make recommendations for how useful these tests might be in clinical practice.

The aim of the research study was to assess drinking during pregnancy in women in the UK by using an online self-report questionnaire. This is an emotive topic and there is a lot of social stigma attached to it, and because of this, this study was done anonymously in the hope of gathering more accurate information. A further aim of this study was to explore women's attitudes and knowledge towards drinking during pregnancy in the UK and how an information leaflet might have an impact on these. This study wanted to know how women in the UK felt about the guidance to abstain from drinking during pregnancy and how knowledgeable they were about the risks.

Results

Results of the systematic review found that the rate of babies exposed to alcohol in second and third trimester of pregnancy varied widely between the studies, from 2.4% to 44%. Studies were from different countries around the world and were quite different in the samples of women they recruited, and the way meconium was collected, stored and tested. It was not feasible to group studies together to get an indication of the prevalence worldwide, however findings did suggest that meconium testing could be helpful for detecting drinking in pregnancy.

Over 1,500 women in the UK took part in the online research study from July to December 2020. Results found that the majority (82%) of women were drinking heavily before they found out they were pregnant, although this decreased significantly after they found out. Still, 25% of women reported drinking during their pregnancy after they had found out. The impact of the information leaflet was significant, as after reading this, women were more strongly opposed to drinking in pregnancy and were more knowledgeable about the risks associated with drinking such as miscarriage, birth deficits and lower IQ.

Conclusions

Findings of the review were helpful as they demonstrated that meconium testing is a useful and objective way of gathering information on alcohol exposure, however more research is needed before using such tests routinely in clinical practice. The research study demonstrated that 25% of women continued to drink during pregnancy, and the information leaflet was helpful in changing women's attitudes towards drinking and improving their knowledge of the risks. This is important as the risks of drinking are high, and by raising awareness and informing women of the risks we can help to reduce drinking during pregnancy. This in turn would help to decrease the rate of FASD and alcohol-related harm to mother and baby, as well as reduce the burden of this on individuals, their families and on healthcare systems. Recommendations to use such leaflets in clinical practice are made.

List of abbreviations

Abbreviation	Explanation
PAE	Prenatal Alcohol Exposure
PAU	Prenatal Alcohol Use
FAS	Foetal Alcohol Syndrome
FASD	Foetal Alcohol Spectrum Disorder
FAEE	Fatty Acid Ethyl Ester
EtG	Ethyl Glucuronide
EtS	Ethyl Sulfate
BI	Brief Intervention

Chapter 1: Systematic Review

The international prevalence of prenatal alcohol exposure obtained via meconium biomarkers: A systematic literature review

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Abstract

Background: Alcohol is a well-known teratogen and its consumption during pregnancy is a growing public health concern across the globe. Ascertaining the true extent of this remains a major challenge however as maternal self-reports may lack validity. Objective measures have gained increasing attention over recent years and meconium is recognised as a valuable tool to detect prenatal alcohol exposure. This review assesses the international prevalence of PAE as obtained using meconium biomarkers in general maternity populations.

Methods: A comprehensive search of the literature for studies reporting the prevalence of prenatal alcohol exposure as determined by meconium biomarker testing was conducted using multiple electronic databases from 1990 to February 2021. Twelve studies were identified for inclusion and evaluated for methodological quality.

Results: The prevalence of PAE as measured using FAEE meconium biomarkers varied widely from 2.4% to 44%. Rates based on EtG analysis ranged from 2.9% to 15%, and EtS analysis from 7.8% to 16.7%. Studies were of moderate quality, although high heterogeneity was observed. Prevalence rates based on self-report data ranged from 0.5% to 37%.

Conclusions: Large variations in prevalence rates reflected the diverse nature of the individual studies and differences in sociodemographic and methodological characteristics. Meconium appears to be a promising objective tool for the detection of PAE but requires methodological rigour and adherence to stringent protocols for sample collection, storage and analysis. Caution should be used when interpreting prevalence rates based on meconium screening, and further research is warranted to develop consistent guidance on the ascertainment, analysis and reporting of meconium samples.Furthermore, the ethical challenges of meconium screening should be considered due to the significant impact these have on public health advice. Implications for clinical practice and recommendations for public policy are discussed.

Keywords

Biomarkers; Meconium; Prenatal; Alcohol; Prevalence; Systematic Review

Introduction

Prenatal alcohol consumption

Alcohol consumption is a part of the social landscape for many societies; however, it is also a significant global health concern, and harmful use is accountable for 5.1% of the global burden of disease (World Health Organisation [WHO], 2018). Prevalence rates have markedly increased between the years 1990 and 2017, particularly in lower- and middle-income countries including India, China and Vietnam (Manthey et al., 2019), although the heaviest rate of drinking is currently observed in Europe (WHO, 2018). Contributing factors to this in Western Europe include greater social acceptance around alcohol use and minimisation of the associated risks. The epidemiology of alcohol use has also changed and there has been a generational increase in consumption among younger cohorts of both men and women (Slade et al., 2016).

Of particular concern is the level of alcohol consumption in women of reproductive age and more specifically during pregnancy, otherwise known as prenatal alcohol use (PAU). 2019). Alcohol is a well-established teratogen, and its consumption during pregnancy places the foetus at risk of congenital malformations and birth defects. Prenatal alcohol exposure (PAE) increases risks of low birth weight, miscarriage, preterm births and perinatal mortality, and is the direct cause of Foetal Alcohol Spectrum Disorder (FASD) (NIAAA, 2021); an umbrella term for a range of cognitive, behavioural and neurodevelopmental deficits observed as a result of PAE. Alarmingly, PAU is a relatively common and socially pervasive behaviour despite public health initiatives to reduce and eliminate PAU, and widespread recommendations in many countries for women to abstain from alcohol during pregnancy.

Prevalence of PAU and FASD varies across the globe. One systematic review conducted by Popova et al. (2017) estimated that the global prevalence of Fetal Alcohol Syndrome (FAS; the most severe form of FASD) in the general population was 14.6 per 10,000 individuals. The authors found the global prevalence estimate of PAU to be approximately 10%, with one in every 67 of these babies exposed to alcohol having FAS. They also demonstrated that Europe has the highest prevalence of FAS as one quarter of women drink during pregnancy. High prevalence equates to high costs, and the economic consequences are substantial, with annual costs of a child with FASD estimated at $22,810, and an overall

estimated cost of over £2 billion in the UK per year (National Institute for Health and Care Excellence [NICE], 2019).

However, these existing estimates are likely to be an under-representation of the full economic burden on individuals with FASD, their caregivers, and society (Greenmyer et al., 2018). FASD presents as a wide range of manifestations, from more subtle impairments to severe developmental delays, and can profoundly impact on a person's functional ability within society (Bryanton et al., 2014). There is a high burden on the individual and their caregivers, as those with FASD are likely to have significant additional needs requiring long-term support (Popova et al., 2011). Extensive literature on the long-term impact of PAE demonstrates that individuals are at a greatly increased risk for numerous secondary adverse outcomes including mental health problems (O'Connor & Paley, 2009), disrupted school experiences, law violations, substance misuse problems, confinement and inappropriate sexual behaviour (Streissguth et al., 2004). Therefore, it is not surprising that providing care for a child with FASD has unique challenges, and studies have indicated high levels of caregiver stress (Bobbitt et al., 2016), isolation, and a perceived lack of support (Mukherjee et al., 2013).

Early identification of PAU, diagnosis of FASD and timely implementation of interventions are all protective factors against such adverse outcomes (McLachlan et al., 2015). However, there appears to be a 'diagnostic dilemma', as PAU and the associated effects are difficult to identify, diagnose and treat (Brown et al., 2011). Research on the epidemiology of PAU and FASD is constrained by the different methodology and diagnostic criteria used (Andrew, 2011), and as a result prevalence and incidence data on PAU and FASD is not well understood.

Screening and assessment of PAU

Research has continued to explore various methods of ascertaining information on PAU in order to assess the true extent of this, and subsequent prevalence of FASD. The reference standard for identifying PAU is maternal self-report. These subjective measures obtain maternal history and information on PAU through discussion between the mother and healthcare professional, and/or by use of alcohol screening questionnaires such as: AUDIT/AUDIT-C (Saunders et al., 1993; Bush et al.,1998), T-ACE (Sokol et al., 1989), CAGE (Mayfield et al., 1974) and TWEAK (Russell & Bigler, 1979), to name but a few.

However, prevalence based on maternal self-report is problematic due to the high probability of error, as factors likely to impact accuracy include the potential for socially desirable responding and recall bias, as well as accidental or intentional underreporting. Research has continuously demonstrated that pregnant women commonly underreport alcohol use (Ernhart et al., 1998; Derauf et al., 2003) and, based on alcohol sales data, this gap could be as much as 40% (Boniface and Shelton, 2013). Lack of understanding of alcohol unit measures and drink strength, and shame and stigma associated with PAU are likely contributing factors to underreporting of PAU. This poses significant challenges when determining prevalence as well as establishing risks to the unborn baby, making clinical diagnoses of FASD, and implementing treatment plans.

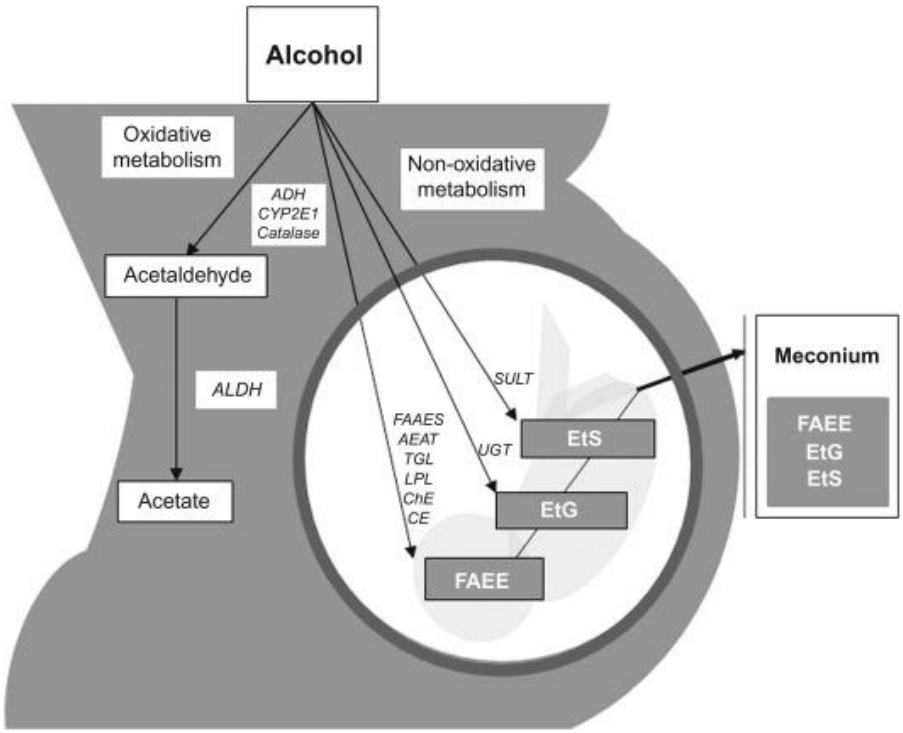
Objective methods have been explored in order to ascertain more accurate prevalence data, and the focus of research over recent years has been to identify and quantify metabolites of alcohol for use in diagnostic and prediction tools (Papaseit et al., 2019). As such, alcohol biomarkers have received growing attention (McQuire et al., 2016). Alcohol metabolites can be detected in a range of biological matrices from the mother (blood, hair, urine, plasma, sweat, oral fluid), newborn (meconium, urine, hair, blood) and from the fetal-maternal exchange (placenta, amniotic fluid and umbilical cord) (Concheiro et al., 2017). With the exception of amniotic fluid, these matrices are advantageous as their collection is non-invasive and can detect prenatal alcohol exposure (PAE) at different gestational periods (Lozano et al., 2007). Amongst these, meconium has been considered the 'gold standard' to detect alcohol and drug exposure in utero (Concheiro-Guisan & Concheiro, 2014).

Metabolites of alcohol and meconium

Meconium is the first stool the newborn passes within 72 hours after birth. Direct metabolites of alcohol can be found within the meconium of newborns as a result of maternal drinking. Meconium starts to form around week 12 of gestation and accumulates during pregnancy until birth, thereby serving as a reservoir of exposure to alcohol and drugs during second and third trimesters. The last trimester (weeks 28-40) in particular produces 75% of meconium (Bakdash et al., 2010). Alcohol goes through oxidative and non-oxidative metabolic processes to produce fatty acid ethyl esters (FAEEs), ethyl glucuronide (EtG) and ethyl sulfate (EtS) (as illustrated in Figure 1). These are then stored for longer periods than the alcohol itself in body fluids and tissues.

Figure 1

Illustration from Papaseit et al. (2019) on the Process of Alcohol Metabolism during Pregnancy and Meconium Biomarkers (used with permission)



Note. This article was published in "*Neuroscience of Alcohol: Mechanisms and Treatment"*, Chapter 60, Papaseit, E., Muga, R., Zuluaga, P., Sanvisens, A., & Farré, M. *Meconium Biomarkers of Prenatal Alcohol Exposure*, page 587, Copyright Elsevier (2019)

Meconium biomarkers do not cross the placenta and therefore represent alcohol metabolised within the foetus (Goh et al., 2010). High levels of FAEE's have been documented in the meconium of babies of women who drank heavily during pregnancy (Bearer et al., 2003, Chan et al., 2003). Research has illustrated that meconium FAEE analysis has a fivefold increase in sensitivity over self-report methods (Gareri et al., 2008) and has demonstrated 100% sensitivity and 98% specificity when a cumulative cut-off of 2.0 nmol/g is used (Chan et al., 2003). EtG and EtS have also been identified as valid biological markers, although there are less published reports on these in comparison to FAEE (Himes et al., 2015). Research has shown that concentrations of EtG >30ng/g have high rates of sensitivity and specificity in identifying regular PAU (82% and 75%, respectively) and has shown moderate correlation to

self-reported PAU (k = 0.57, 95% CI 0.4 – 0.7) (Himes et al., 2015). Meconium EtS is less well-established as a marker of PAU compared to EtG, although is considered a useful biomarker (Bager et al., 2017). A review conducted on the diagnostic accuracy of biomarkers concluded that meconium screening is a promising tool for detecting PAE, although further larger scale research on population samples is still required (McQuire et al., 2016). Nevertheless, meconium is an easily obtainable non-invasive neonatal screening tool for identifying PAE and biomarkers have been shown to provide more accurate data than maternal self-reports/questionnaires (Papaseit et al., 2019).

Rationale & research questions

Obtaining reliable information on PAU is challenging as methods to detect PAE are constrained by a multitude of factors. Predominantly research has focused on the utility of maternal self-reports for identifying infants at risk of alcohol exposure, however they are limited by reporting and recall bias and likely to result in an underestimation of prevalence rates for PAU and FASD. Objective measures such as meconium biomarkers may prove more accurate in determining prevalence of PAE. One previous systematic review compared the prevalence of PAU via meconium and maternal self-reports (Lange et al., 2014), however it included studies that recruited from high-risk antenatal settings such as neonatal intensive care units (Pichini et al., 2009; Manich et al., 2011) and high-risk obstetric units (Goh et al., 2010). Research has demonstrated that infants born in high-risk settings are at greater risk of screening positive for PAE (Goh et al., 2010), thus potentially compromising the generalisability of findings.

The objective of this review was to identify the prevalence of PAE as obtained using meconium biomarkers of alcohol including FAEEs, EtG & EtS in general maternity settings. Additionally, a major focus of governments and public health bodies globally over recent years has been on the prevention and identification of PAE in order to facilitate diagnosis of FASD and implement interventions. More research exploring the utility of meconium biomarkers as a valid method of assessing PAE has been published over recent years, and this review aims to update the literature on prevalence with the hope of informing policy and recommendations for its utility.

The following research questions were addressed:

1. What is the international prevalence of PAE in representative maternity populations as indicated by meconium biomarkers?
2. What is the prevalence of PAE as indicated by meconium FAEE's, EtG and EtS biomarkers independently?
3. What is the variance in prevalence by geographical location?

Method

This systematic review was conducted in accordance with Preferred Reporting Items for Systematic Reviews and Meta-Analyses standards (PRISMA; Moher et al., 2009), and adhered to the principles recommended by the Centre for Reviews and Dissemination (CRD, 2009). Prior to formal screening a protocol was registered on PROSPERO international prospective register of systematic reviews and is available at https://www.crd.york.ac.uk/prospero/ (record number: CRD42021229732).

Information sources and search strategy

A literature search was conducted to identify published and unpublished studies that investigated the prevalence of prenatal alcohol exposure in general maternal populations using meconium biomarkers. Scoping searches were initially conducted between December 11th 2020 and January 17th 2021, and the final search was conducted on February 10th 2021. The following electronic bibliographic databases were searched: APA PsycInfo, Embase Classic+Embase, Ovid MEDLINE(R) and Epub Ahead of Print, In-Process & Other Non-Indexed Citations and Daily, ProQuest Dissertations and Thesis Global, Cumulative Index to Nursing and Allied Health Literature (CINAHL Plus), Scopus and OpenGrey. References of included full-text studies were examined for additional relevant literature. Searches were limited to English language publications published since 1990, and animal studies were excluded.

The search was conducted utilising numerous combinations of the following key words: 1) Prevalen*, epidemiolog*, frequenc*, occur*, inciden*, probability, rate* OR statistic*; AND 2) Prenatal, pregnan*, antenat*, postnat*, primigravida, expect* mother*, matern*, maternal-fetal exchange, infant, newborn*, baby; AND 3) Alcohol*, ethanol, binge drinking, ARBD, ARND, drunk*, FAS, FASD, Intoxicat*, PAE OR pFAS; AND 4) meconium, FAEE, "alcohol metabolite*", "fatty acid* ethyl ester*", EtG, "ethyl glucuronide*", “ethyl sulfate” OR EtS (see Appendix B for terms utilised for each database).

If published abstracts were deemed relevant but full texts of the studies were not yet published/available, authors of studies were contacted to provide additional information to include within the analysis. A specified time limit of four weeks was given for authors to

respond. Studies were excluded on the basis of lack of specified criteria if no further information was provided.

Eligibility criteria

Articles were retained if the following inclusion criteria were met: (i) observational study designs including retrospective and prospective cohort studies and cross-sectional studies; (ii) original and quantitative in nature and published in a peer-reviewed or scholarly report; (iii) report an estimated prevalence of prenatal alcohol exposure or report results which allow for its calculation; (iv) prevalence must have been measured by meconium biomarkers; (v) Population of pregnant/post-partum women and/or neonates in general maternity settings.

Articles were excluded if they were:
(i) Animal studies, individual case studies, and studies which did not provide data to assess primary outcomes, or which included secondary analysis of data; (ii) Review studies or meta-analyses; (iii) Studies reporting a pooled estimate of PAE by combining several studies; (iv) specific populations not representative of the general population, such as substance use populations, neonates born in high-risk obstetric/antenatal units (v) Studies published in iteration i.e., if papers were subsequent publications of results already included.

Study selection

Following de-duplication of the studies returned from the searches, titles and abstracts were screened for eligibility by the first and third author. For abstracts and publications deemed relevant, full texts were retrieved or requested. Additionally, for studies where the title and abstract lacked sufficient information to determine its inclusion or exclusion, the full text was retrieved. Both reviewers assessed relevance of studies as per the inclusion criteria stated above, and any discrepancies were resolved by discussion. Studies that did not meet criteria were excluded. Full-text screening for eligibility was completed for 64 articles. Inter-rater reliability was calculated at both stages of screening. The level of agreement as indicated by Cohen's Kappa was 0.88 at the title and abstract screening stage, and 0.94 at full-text stage indicating almost perfect agreement between reviewers. Where there were any differences, these were discussed between reviewers and an agreement reached.

Data extraction

Following de-duplication of studies, study selection was completed by initially screening titles and abstracts for inclusion, followed by screening of all remaining relevant full-text articles. The lead reviewer screened first, followed by the third author. Disagreements were resolved through discussion in order to reach a consensus.

Following quality assessment of included studies, data extraction was completed systematically by the lead author. The primary reviewer independently extracted the data from included articles, and for accuracy, the second reviewer checked table entries.

The following data was extracted, where available: first author, title, year of publication, journal, study design, aims, population characteristics (women and/or newborn infants), country/location of recruitment, study setting, the year(s) in which data collection took place, prevalence/incidence of PAE (n, %) via self-reported data (n, % & 95% confidence intervals), assessment tool used to obtain self-report PAU, level of agreement, maternal sample characteristics (age, sample size, socio-economic status, ethnicity, level of education), trimester of PAE, infant sample characteristics (sex, sample size, ethnicity, gestational age at delivery [in weeks], head circumference, length in cm at birth), biomarker utilised, estimates of prevalence/incidence of PAE via meconium testing (n, % & 95% confidence interval), cumulative FAEE cut-off concentration used, EtG & EtS cut-off, details of collection, analysis used, testing and storage of meconium, inclusion and exclusion criteria, primary outcome and secondary outcomes.

Evaluation of methodological quality

Methodological quality and risk of bias was assessed with a tool specifically employed for systematic reviews addressing questions of prevalence; the "Joanna Briggs Institute Critical Appraisal Checklist for Studies Reporting Prevalence Data" (Joanna Briggs Institute [JBI], 2017). Developed by Munn et al. (2015), this checklist comprises nine items, each with four standard answer options, and a further item for the overall appraisal of the study based on the rater's judgement. A systematic review comparing all available instruments designed to appraise risk of bias for prevalence studies concluded that the JBI tool was the most appropriate with higher methodological rigour than its counterparts (Migliavacha et al., 2020).

The tool was used to guide evaluation of included studies across the following criteria: representative sample frame, appropriate recruitment, adequate sample size, detailed description of study subjects and setting, data analysis, methodology used, validity of methodology, reliability of measurement of the condition of interest, appropriate statistical analysis and adequate response rate. Study quality was independently assessed by both reviewers to ensure consistent application of the tool and to improve validity and accuracy. Discrepancies were resolved by clarifying details of the items and a consensus reached via discussion. No studies were excluded based on the quality assessment.

Statistical analysis

The review aimed to establish a pooled estimate of the prevalence of PAU as indicated via meconium biomarkers. Data on prevalence was gathered from all included studies and assessed for heterogeneity prior to analysis.

Results

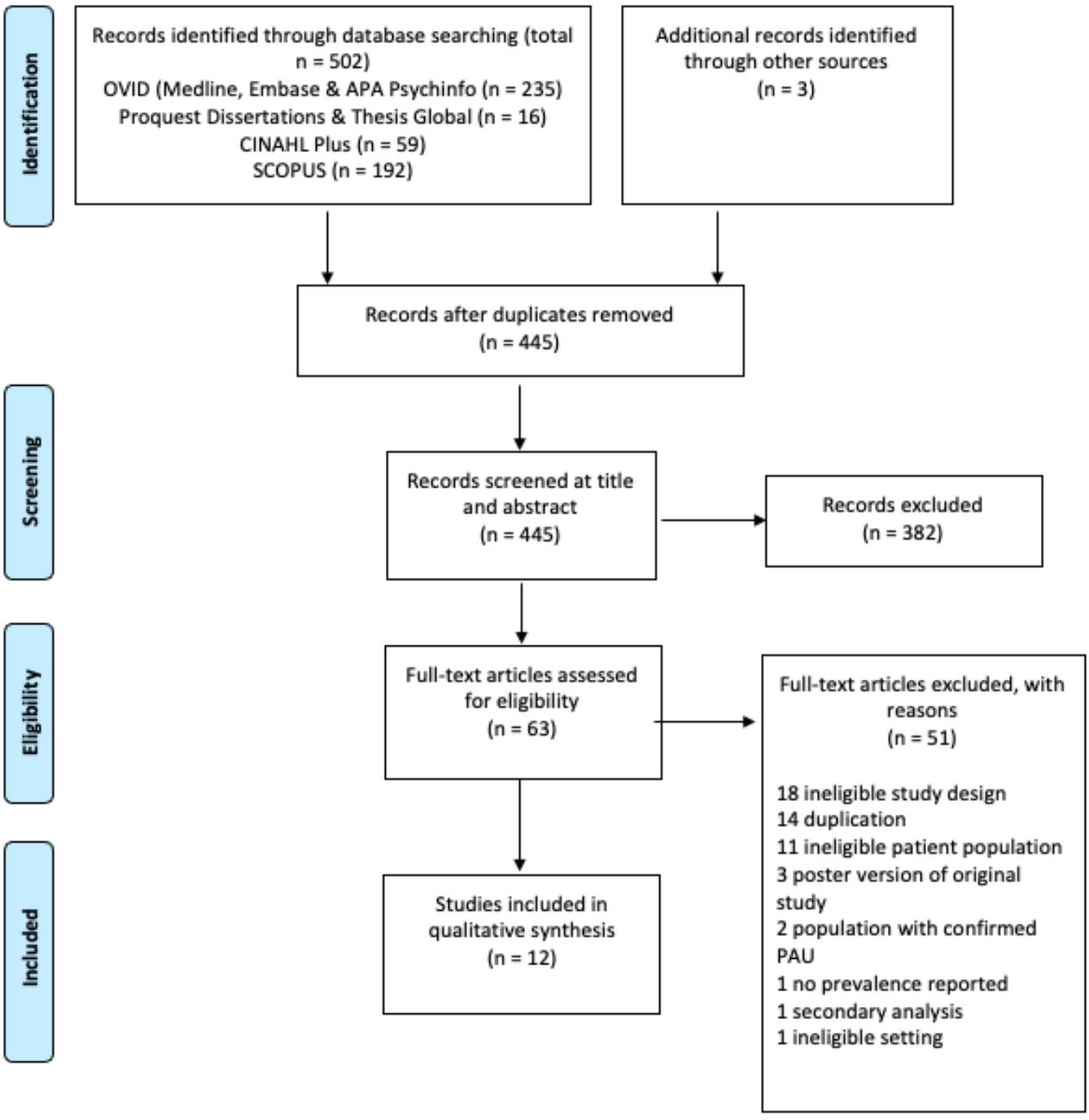
Search results

Electronic searches and additional sources yielded a total of 505 citations. Following removal of duplicates (*n* = 58), 445 citations were screened using title and abstracts. A further 382 records were excluded at this stage as they did not meet inclusion criteria. Subsequently, 63 full-text articles were assessed for inclusion, 49 of which were excluded. A total of 12 studies fulfilled the inclusion criteria and were retained for data extraction. A schematic diagram is illustrated below in Figure 2.

Importation of citations and screening and exclusion of records were managed using the Covidence Systematic Review Management Software (https://www.covidence.org/). Two of the included studies at the data extraction stage were found to be duplicated data: Nightingale (2016) was a doctoral dissertation of a published study (English et al., 2016) published in iteration, and therefore studies were merged and reported as a single study. Similarly, Derauf et al. (2003) and Moore et al. (2003) were merged as following data extraction and contact from the original author, the data was confirmed to have been reported on the same sample.

Figure 2

Systematic Literature Search and Study Selection Process Illustrated using PRISMA Flow Diagram (Moher et al., 2009)



Characteristics of included studies

Key characteristics

Study characteristics and demographic information are summarised in Tables 1 and 2. All studies were published in peer review journals. One study was published in 2003 (Derauf et al., 2003) and the remaining between 2010 and 2019. Studies included data on prevalence across four continents including Europe, North America, South America and Africa. Study designs were cross-sectional population-based studies or cohort studies, with one being voluntary in nature (Delano et al., 2019).

Maternal characteristics

Samples were recruited from maternity settings such as general hospitals, prenatal clinics, birthing hospitals, neonatology wards or obstetrics units. In terms of characteristics of maternal samples, nine studies reported age ranges of the mothers in the studies. Ages ranged from 24.9 years (English et al., 2016) to 32.3 years (Bana et al., 2014). Sociodemographic factors were reported inconsistently as only half of the studies reported either socioeconomic status (SES), income or employment status. The samples of two studies had low SES (Abernethy et al., 2018; Hutson et al., 2010), the majority of one sample earned less than $19,999 per annum (Bakhireva et al., 2019), whilst the majority of another study (Delano et al., 2019; 57.8%) had an income of >$80,000. Employment rates were 72% in Bana et al. (2014) and 75.4% in Lamy et al. (2017).

Five studies reported information on the level of education obtained and marital status. The majority of the women recruited in three of these studies had completed secondary/high school and/or college/university degree: 73.7% in Bakhireva et al. (2019); 72% in Bana et al. (2014); and 54.5% in Lamy et al. (2017). In comparison, 55% of women in English et al. (2016) were categorised as having primary/no education, and 95% of Hutson et al. (2010) had completed less than secondary level education. Regarding marital status, the vast majority of women in three studies were married or cohabiting: 83.5% in Bakhireva et al. (2019), 95.3% in Delano et al. (2019), and 94% in English et al. (2016). Whereas in Hutson et al. (2010) only 18% of the sample were married.

The use of tobacco varied greatly amongst the studies, as well as the manner in which this was reported. Some studies specified prevalence rates of tobacco use during pregnancy: 13.3% (Derauf et al., 2003), 5.9% (Delano et al., 2019), 0.2% (English et al., 2016) and 17.1% during the 3rd trimester (Lamy et al., 2017). Others reported tobacco use but did not specify whether this was during pregnancy or prior to (Abernethy et al., 2018; Hutson et al., 2010; Sanvisens et al., 2016).

Information on whether the mother had had previous pregnancies or births prior to the one reported on in the study was also collected by half of the studies. The rate of women who had never given birth ranged from 29.7% (Bakhireva et al., 2019) to 44% (Delano et al., 2019), and those who were pregnant for the first time (primigravida) ranged from 9.9% (Pichini et al., 2012) to 40.4% (Delano et al., 2019).

Infant characteristics

All samples were neonates born in maternity settings. Infants born in high-risk settings were excluded. Mean gestational age of delivery was similar across studies that detailed this (*n* = 5) and ranged from 38.7 weeks (Bakhireva et al., 2019) to 39.7 (Abernethy et al., 2018). Average birth weights were also similar and ranged from 3.25kg (Pichini et al., 2012) to 3.46kg (Abernethy et al., 2018).

Table 1

Study Characteristic Table

Study	Year of publication	Country, province/territory or state (if available)	Design	Aims	Inclusion criteria	Exclusion criteria
Abernethy	2018	Scotland, Glasgow	Observational, cross sectional, population-based study	To investigate the feasibility of determining the pattern and prevalence of alcohol consumption in pregnancy by measuring ethanol biomarkers (FAEE &EtG) in meconium.	All mothers delivering singleton infants born after 36 completed weeks' gestation, during every eighth 24-hour period over 5 months	Multiple births
Bakhireva	2019	New Mexico	Birth cohort study	To estimate PAE prevalence among newborns in the Navajo Nation, using ethanol biomarkers measured in meconium.	Pregnant women: (a) age: 14–45 years, (b) lived on Navajo Nation for at least 5 years at any time in their life, (c) agreed to receive prenatal care and deliver at one of five participating hospitals and (d) willing to have their child followed-up for biological sample collection and developmental assessment through the first year of life	NS
Bana	2014	Spain, A Coruna	Prospective cohort study	To determine the prevalence of the positive biomarkers of alcohol in newborns with PAE and establish the analytic procedures to identify EtG and FAEEs in meconium as a routine practice.	Neonates ≥32 weeks of gestation and/or ≥1500 g weight at birth and in health area	Babies with major malformations or severe diseases, or consent refusal from the parents
Bryanton	2014	Canada, Prince Edward Island	Anonymous birth cohort study	To establish the incidence of PAE via analysis of meconium samples.	All neonates born to women in PEI over a 1-year period	NS

Delano	2019	Canada	Birth cohort study	To estimate the prevalence of heavy PAE via analysis of meconium FAEEs.	Women aged 18 years or older; <14 weeks gestation; ability to communicate in English or French; plan to deliver at a local hospital; and willingness to provide a cord blood sample.	Any known fetal chromosomal abnormalities or major malformations in the current pregnancy, and/or a history of medical complications including epilepsy, hepatitis, cancer, hematological disorder, threatened spontaneous abortion, illicit drug use, or disease of major organs (heart, kidney, liver, lung).
Derauf	2003	US, Hawaii	Observational, population-based study	To assess agreement between maternal self-reported tobacco use and PAU and detection of metabolites associated with tobacco use (cotinine) and ethanol intake (FAEE)	All newborns delivered in centre in Nov-Dec 1999	NS
English	2016	Uganda, Mbarara	Cross sectional, population-based study	To assess the prevalence and predictors of PAU in Southwestern Uganda.	All pregnant women presenting to the maternity ward at in active labour between September 23 and November 23, 2013 were eligible for enrolment. All consented neonates born during the 2 months. An equal number of rural and urban mothers were enrolled in the study, therefore after reaching the quota for a certain demographic (rural or urban), only women of the remaining demographic were permitted to be included in the study.	If (1) the child died following delivery or was transferred to another ward where meconium collection was not possible; (2) the mother–child pair was discharged prior to the passing of the first meconium; or (3) the mother was sufficiently ill to preclude adequate informed consent, as deemed by study personnel.
Gareri	2008	Canada, Ontario	Cross sectional, population-based study	To establish an objective PAE prevalence value and compare results with the rate of PAU as obtained in self-reported PAU.	All neonates born within a 12-month period at each birthing site in the region of Grey Bruce	Neonates born to women living outside the region and all neonates whose mothers refused to

						provide a meconium sample
Hutson	2010	Uruguay, Montevideo	Cross sectional study	To determine the incidence of PAE in the public health care sector in Montevideo, Uruguay, using FAEE in meconium.	The mother had to be in good health, between the ages of 13 and 45 years, and had to provide written consent	Twins or subjects with missing data
Lamy	2017	France, Normandy	Cross sectional, population-based study	To compare the prevalence of alcohol, tobacco and/or cannabis use during the third trimester of pregnancy (using maternal self-reports) with the results of meconium testing of their metabolites in newborns (cotinine, ethyl-glucuronide (EtG) and cannabinoid metabolites)	Any pregnant women aged 18 or over and living in catchment area that delivered a child in one of three maternity hospitals, was included	269 deliveries were not included for the following reasons (sometimes for several reasons): 61 mothers declined to participate, 48 did not speak and/or understand French language, 6 were younger than 18 years, 145 were living outside catchment area, 12 left the maternity hospital before inclusion, 2 had a critical illness at inclusion, stillbirths occurred in 6 cases, and one mother delivered anonymously.
Pichini	2012	Italy	Cross sectional, population-based study	Multi-centre study to assess PAU by objective measurement of meconium biomarkers	All term neonates born in the center during an established time period (usually about 1 month, with the exception of Reggio Emilia, where collection lasted 3 months)	Those with severe pathologies requiring intensive care (8 newborns were excluded)
Sanvisens	2016	Spain, Barcelona	Cross sectional study	To analyse prevalence of alcohol consumption in mothers and PAE.	A series of parturient women who were admitted to the Obstetric Unit between Sept 2011 and March 2012	NS

Note. NS = not specified

Table 2

Participant Characteristic Table

				Maternal characteristics					Infant characteristics	
Author	**Population**	**Setting**	**Sample size**	**Age in years; M (SD)**	**SES/Income/ Employment Status**	**Level of education**	**Marital status**	**Tobacco use**	**Parity/gravidity**	**Gestational age at delivery in weeks; M (SD)**	**Birth weight in kg; M(SD)**
Abernethy	Random sample of singleton newborns	Maternity hospital in Scotland	325	29.9 (5.0)	Low SES; DepCat score 6/7	-	-	19% smoker	43% primiparous	39.7(1.3)	3.46(0.5)
Bakhireva	Cohort newborns	5 hospitals in Arizona & New Mexico	570	27.4(6.0)	71.3% <$19,999 per annum, 10% $20,000-39,999, 3.3% >$40,000	22.4% <high school grad, 32.9% high school grad/GED, 40.8% college/vocation or higher	83.5% married/cohabiting, 7.6% separated/divorced, 8.9% single	1.8% regular use, ceremonial purposes only 35.9%	29.7% nulliparous, 25.6% primigravida	38.7(1.8)	3.36(0.5)
Bana	Random sample of newborns	Maternity ward of hospital in Spain	110	32.3 (3.9)	72% working, 16% unemployed, 12% housewife	27% primary education, 55% secondary education, 17% university education	-	-	-	-	-
Bryanton	Consecutive newborns	3 General hospitals in Nova Scotia	1307	-	-	-	-	-	-	-	-
Delano	Volunteering women	Prenatal clinics across 10 cities in Canada	2001	32.2(5.1)	3.9% <$20k, 18.6% $20-60k, 14.9% $60-80k, 19.6% $80-100k, 38.2% >$100k	-	95.3% married/common law, 0.4% divorced/separated, 4.2% single	5.9% current smoker, 6.1% quit during pregnancy, 61.7% never smoked,	44% nulliparous, 40.4% primigravida	39.2(1.9)	3.40(0.6)

								26.3% former smoker			
Derauf	Consecutive newborns	Large urban regional perinatal centre in Hawaii	546	-	-	-	-	13.3% during pregnancy	-	-	-
English	Mother-child dyads	Maternity ward in Uganda	505	24.9 (5.8)	41% rural (village), 47% urban (city), 12% semiurban (trading center)	55% primary/no education, 30% secondary education, 15% post-secondary education	94% married/cohabiting, 6% single	0.2 % current smoker	Mean of 2 previous pregnancies (SD=1-3)	-	-
Gareri	Newborns	5 regional birthing hospitals in Ontario	1076	-	-	-	-	-	-	-	-
Hutson	Newborns	2 public hospitals in Uruguay	900	25.35	Low SES, 84% unemployed	95% <secondary level education, 11% < primary level education, 0.9% university	18% married	42%	-	-	-
Lamy	All women that delivered a child	Maternity hospitals in France	724	Mdn=29.6 [IQR=18.7-44.2]	75.4% employed	54.5% university degree	7 (1%) living alone	17.1 % during 3rd trimester	-	39.5(1.5)	3.35(0.5)
Pichini	All term newborns	Neonatology wards of 7 public hospitals in Italy	607	32.1 (5.4)	-	5.7% manager,7.6% partly skilled, 26.9% skilled, 30.9% unskilled	-	-	9.9% primigravida, 64.2% multigravida	-	3.25(0.51)
Sanvisens	A series of parturient women	Obstetric Unit at Hospital in Spain	51	Mdn=30 [IQR=26-34]	-	-	-	12%	43.1% nulliparous, 45.1% primiparous	Mdn= 40 [IQR 38.9-41]	Mdn = 3.24(IQR = 3.05-3.67)

Note. Median and interquartile ranges (Mdn & IQR) recorded in some cases

Methodological quality review

The agreed ratings for each item on the quality assessment tool are displayed in Table 3. The number of criteria met ranged from three (Sanvisens et al., 2016) to eight and the average criterion fulfilled was six out of nine. Two studies fulfilled eight out of nine criteria (Hutson et al., 2010 & Lamy et al., 2017).

Table 3

Study Quality Criteria Ratings

Study	Representative sample	Appropriate recruitment	Adequate sample size	Subjects & setting described	Sufficient data analysis	Appropriate methodology	Reliable measurement	Appropriate statistical analysis	Response rate described
Abernethy (2018)	✓	✓	✓	✓	*NA*	✓	✓	✗	✓
Bakhireva (2019)	✓	✓	✓	✓	*NA*	✓	✓	✓	✗
Bana (2014)	✓	✓	✗	✓	*NA*	✓	*UN*	*UN*	✓
Bryanton (2014)	*UN*	✓	✓	✗	*NA*	✓	✓	✓	✓
Delano (2019)	✓	✓	✓	✗	*NA*	✓	✓	✓	✓
Derauf (2003)	*UN*	✓	✓	✗	*NA*	✗	✓	*UN*	✓
English (2016)	✓	✓	✓	✓	*NA*	✓	*UN*	*UN*	✓
Gareri (2008)	*UN*	✓	✓	✗	*NA*	✓	✓	✓	✓
Hutson (2010)	✓	✓	✓	✓	*NA*	✓	✓	✓	✓
Lamy (2017)	✓	✓	✓	✓	*NA*	✓	✓	✓	✓
Pichini (2012)	✓	✓	✓	✓	*NA*	✓	✓	✗	*UN*
Sanvisens (2016)	✓	*UN*	✗	✗	*NA*	✓	✓	*UN*	✗

Note. ✓ Yes (item adequately addressed); ✗ no (item not adequately addressed); *UN* unclear (item not stated); *NA* not applicable

In terms of methodological strengths within included studies, three out of four studies were deemed to have a representative sample. Although the majority of studies did not report sample size calculations, the reviewer conducted these as per the quality assessment tools guidance on epidemiological studies using Naing et al.'s (2006) statistical formula. Using the prevalence of PAU rate of 18.9%, as obtained via meconium measures in a systematic review and meta-analysis conducted by Popova et al. (2017), a minimum sample size of 236 was required. All studies with a sample of 236 or above therefore met this criterion, which equated to 80% of studies in this review.

A major strength noted during the quality appraisal process was the clear description for the rationale of each study and its main objectives. Furthermore, all studies, with the exception of Sanvisens et al. (2016), demonstrated appropriate recruitment of the sample and described this in a comprehensive manner. Random sampling methods were employed by two studies (Abernethy et al., 2018 & Bana et al., 2014), whilst nine others utilised consecutive sampling over a designated time period. Appropriate description of response rates was provided for all studies with the exception of Bakhireva et al. (2019), Pichini et al. (2012) and Sanvisens et al. (2016). Additionally, inter-rate reliability of the quality appraisal indicated almost perfect agreement between reviewers, as demonstrated by a Cohen's Kappa value of 0.87. Discrepancies were resolved via discussion.

Methodological weaknesses were also observed; five of the studies failed to describe the sample or setting in sufficient detail (Bryanton et al., 2014; Derauf et al., 2003; Delano et al., 2019; Gareri et al., 2008; Sanvisens et al., 2016). One quarter of studies did not specify exclusion criteria (Bakhireva et al., 2019; Bryanton et al., 2014; Derauf et al., 2003; Sanvisens et al., 2016). A major concern noted was the inconsistency in the reporting of prevalence data, and how rates and proportions were calculated. Different units of measurement of PAE and cut-off points, as well as different expressions of prevalence data were complicating factors in the included studies and limited the ability to draw comparisons across studies. 50% of the studies either did not conduct appropriate statistical analysis as they did not utilise recommended cut-off points for analysis or were unclear in their reporting of methodology and analytical strategies utilised (Abernethy et al., 2018; Bana et al., 2014; Derauf et al., 2003; English et al., 2016; Pichini et al., 2012; Sanvisens et al., 2016). Only three of the quality criteria were met in Sanvisens et al. (2016); this study did not demonstrate adequate sample

size or management of response rate and failed to provide adequate description of the study subjects and setting.

Even within studies analysing FAEE's alone, there was no consensus on the number of FAEE's summed to calculate prevalence, and some studies did not specify this in their methodology. Furthermore, the 'limit of detection' (LOD), i.e., the lowest quantity of a concentration that can be measured was inconsistent with the laboratories conducting these analyses using different reference points (as illustrated in table 4). For example, Gareri et al. (2008) utilised an LOD of 50ng/g, which could have resulted in different prevalence rates if the typical LOD of 100ng/g was used.

The appraisal process highlighted further methodological concerns. Not all studies clearly specified inclusion and exclusion criteria or provided an adequate description of study characteristics and sociodemographic information, thus limiting potential for replicability and transferability of results across cohorts and countries. Additionally, some studies did not specify detailed procedures of meconium collection and storage, thus prohibiting the evaluation of the validity and methodological rigour of the findings of those studies. Meconium samples require careful collection and preservation in order to avoid the possibility of contamination, and improper storage can increase the possibility of false-negative results (Gray & Huestis, 2007). More specifically, FAEEs are sensitive to light and temperature, and samples degrade by approximately 86% within a 24-hour period when stored at room temperature. As such, samples require storage almost immediately following collection, in a -20 ℃ freezer (Moore et al., 2003). The procedures around collection of meconium of studies in this review varied in the detail with which they were reported and conducted, however (as illustrated below in Table 4). In this review, eleven of the studies described storage procedures and only seven of these adhered to this protocol.

The timing of collection is also paramount as one study conducted by Zelner et al. (2012) found that false positive FAEE results can occur as a result of delayed sample collection. The authors proposed that results of meconium analysis should be interpreted with caution for samples passed after the first 24 hours following birth, or samples collected after the first meconium sample was passed, due to the possibility of contamination and elevated FAEE's. Not all samples in this review were collected within the recommended 24-hour period, nor

were they first samples. Only one study specified collection of samples within 24 hours following the birth (Bryanton et al., 2014), although authors noted that not all samples of meconium were the first ones excreted. Lack of information on timing of collection was observed across half of the studies thus highlighting a concern around methodological rigour.

Lastly, the majority of studies (n = 9) required informed consent from the mother for meconium samples to be collected and/or analysed. Exceptions were Bryanton et al. (2014) and Gareri et al. (2008) whereby collection of samples was anonymous and so did not require consent, however once informed of the study post-birth mothers retained the right to withdraw consent. For example, meconium analysis was conducted on 52% of one cohort (Bakhireva et al., 2019). Therefore, it was possible that women who did drink during pregnancy chose not to give consent to the study or to provide samples for collection following consent

Table 4

Study Results Table Reporting Meconium Collection and Storage Procedures

Author	Biomarker	Limits of detection/quantification	Procedure of Meconium Collection/Storage
Abernethy	FAEEs, EtG	LOQ of 10–15 ng/g for FAEEs & 10 ng/g for EtG	Samples collected from disposable plastic bag into anonymised, sequentially numbered containers. First meconium sample was collected where possible, but second sample was accepted if the first had been missed. Samples were frozen at −20°C and transported on dry ice for analysis.
Bakhireva	FAEEs, EtG, EtS	LOD of 1.0 ng/g for EtS & EtG. LOQ of 3.0ng/g for EtS & 5.0 ng/g for EtG. LOD for each FAEE ranged from 10–25 ng/g & LOQ from 15–50 ng/g.	Sample collected from trained staff and placed in a sealed plastic container inserted within a brown paper bag to protect from light. Samples placed in −80C study-specific freezers within 1–1.5 hr from collection (samples stored at 4 C temperature before transfer to ultralow temperature freezers), batched, and shipped on dry ice for analyses.
Bana	FAEEs, EtG	FAEE: LOD of 100ng/g & LOQ of 1000ng/g. EtG: LOD of 20ng/g & LOQ of 50ng/g	Samples of first meconium were collected. Analysis of 500mg of meconium samples were conducted.
Bryanton	FAEEs	LOD of 0.4 nmol/g	Samples were anonymously collected by nursing staff as part of the routine newborn protocol. A minimum of 10 mL of meconium was collected from each live neonate. First meconium sample was collected; however, this was not always possible. Meconium was scraped out of soiled diapers and deposited into 15 g ointment jars. The specimen container was then placed into a biohazard bag and frozen at –20°C within 12 hours of collection. Samples were couriered in a frozen condition on dry ice to laboratory for analysis.
Derauf	FAEEs	NR	The mother and nurse of each enrolled newborn were instructed to place all soiled diapers or other items containing meconium into a crib- side bag during the first 2 or 3 days after birth. These items were collected twice daily from each subject for the duration of the newborn infant's hospitalization. Collected meconium samples were coded anonymously. Samples were placed into a single foil-wrapped container, weighed, frozen at –20°C, and sent in batches (100 samples per batch) to laboratory for analysis.
Delano	FAEEs	LOD of 0.125 ng/g. LOQ of 0.400ng/vial	Meconium collected post-partum at day 1/2. Samples were collected from diapers by an applicator, into a test tube and frozen at -4C. Approx. 500 mg of meconium was apportioned from each sample and transported to laboratory and stored in −80 °C until analysis.

English	FAEEs	NR	Meconium samples were anonymously collected within the first 24-48 hours of life. The research midwife harvested the meconium sample from the soiled diaper and transferred the specimen to a plastic container to be stored in a -20°C freezer. Date(s) and time(s) of collection were specified and if it was the first, second, or third meconium excretion. Samples were transported on dry ice to laboratory. Stored in–80°C freezer until analysis.
Gareri	FAEEs	LOD of each FAEE ranged from 0.16-0.22 nmol/g (approx. 50 ng/g). LOQ of 1.0 mg/mL.	Soiled diapers were placed in a sealable biohazard bag by the mother or local research coordinator and placed in a –20°C freezer onsite. These were collected periodically and transported to the laboratory for analysis where they were thawed and meconium samples scraped into screw cap conical sample collection tubes, coded by location of origin, and stored at –20°C or –80°C.
Hutson	FAEEs	LOD of each FAEE ranged from 0.16-0.22 nmol/g & LOQ ranged from 0.32-0.44 nmol/g.	Meconium samples were collected from infants' diapers, transferred to plastic tubes, and stored at –20°C. After all samples were collected, the meconium was couriered to laboratory on dry ice. Samples were then stored at –80°C until analysis.
Lamy	EtG	LOQ of 40 ng/g. LOD of 60 ng/g.	Meconium was scraped from diapers and immediately transferred into propylene tubes. Each meconium was homogenized and mixed vigorously with methanol, then vortexed and ultrasonicated. After centrifugation at 4 C, supernatants were stored at 20C and then transferred on ice. A weight of 0.2 g of meconium was defined as the minimal weight necessary to proceed with the analyses of the samples.
Pichini	FAEEs, EtG, EtS	LOQ of each FAEE ranged from 0.14- 0.20 nmol/g. LOQ for EtS of 0.008 nmol /g & 0.022 nmol/g for EtG.	Meconium, collected within the first 24 to 48 hours of newborn life, was placed into a plastic tube, homogenized, and immediately stored in aliquots at 20C. One set of aliquots was sent to the Laboratory to measure meconium EtG and EtS concentrations, while the second set was sent to be analysed for FAEEs
Sanvisens	EtG, EtS	NR	Meconium samples were refrigerated at 4 ˝C and frozen at -80C. Aliquots were analysed for EtG and EtG using LC-MS/MS according to a validated method.

Note. LOQ = Limit of quantification. LOD = Limit of detection. NR = Not reported

Meconium analysis and prevalence of PAE

Due to the heterogeneity of the studies, a meta-analysis was deemed inappropriate. Differences across biomarkers utilised and their respective cut-off points, inconsistencies in reporting outcomes, and diversity of protocols surrounding meconium collection and storage procedures precluded a statistical synthesis of the included studies. A narrative synthesis of the data is therefore presented.

Data on the prevalence of prenatal alcohol exposure as obtained using meconium biomarkers are illustrated in Table 5 below. With respect to biomarkers utilised, FAEE's were used to assess prevalence in all but two studies; Lamy et al. (2017) used EtG, and Sanvisens et al. (2016) used EtG and EtS. However, the manner in which prevalence rates were calculated differed between studies. Only five studies employed the internationally accepted cumulative cut-off point for FAEE analysis of 2nmol/g (Bryanton et al., 2014; Delano et al., 2019; English et al., 2016; Gareri et al., 2008; Hutson et al., 2010). Other studies used different measurement units of FAEE, for example Abernethy et al. (2018) used a cut-off point of >600ng/g. Conversion of units demonstrated that based on a molecular weight of 280g/mol, 2nmol/g equates to approximately 560ng/g. Therefore, results of this study were found to be comparable with the previous 5 studies reporting rates in terms of nmolg/g. However, the cut-off used by Bana et al. (2014) at 1000ng/g was much higher than recommended, reflecting the possibility of underestimation of prevalence.

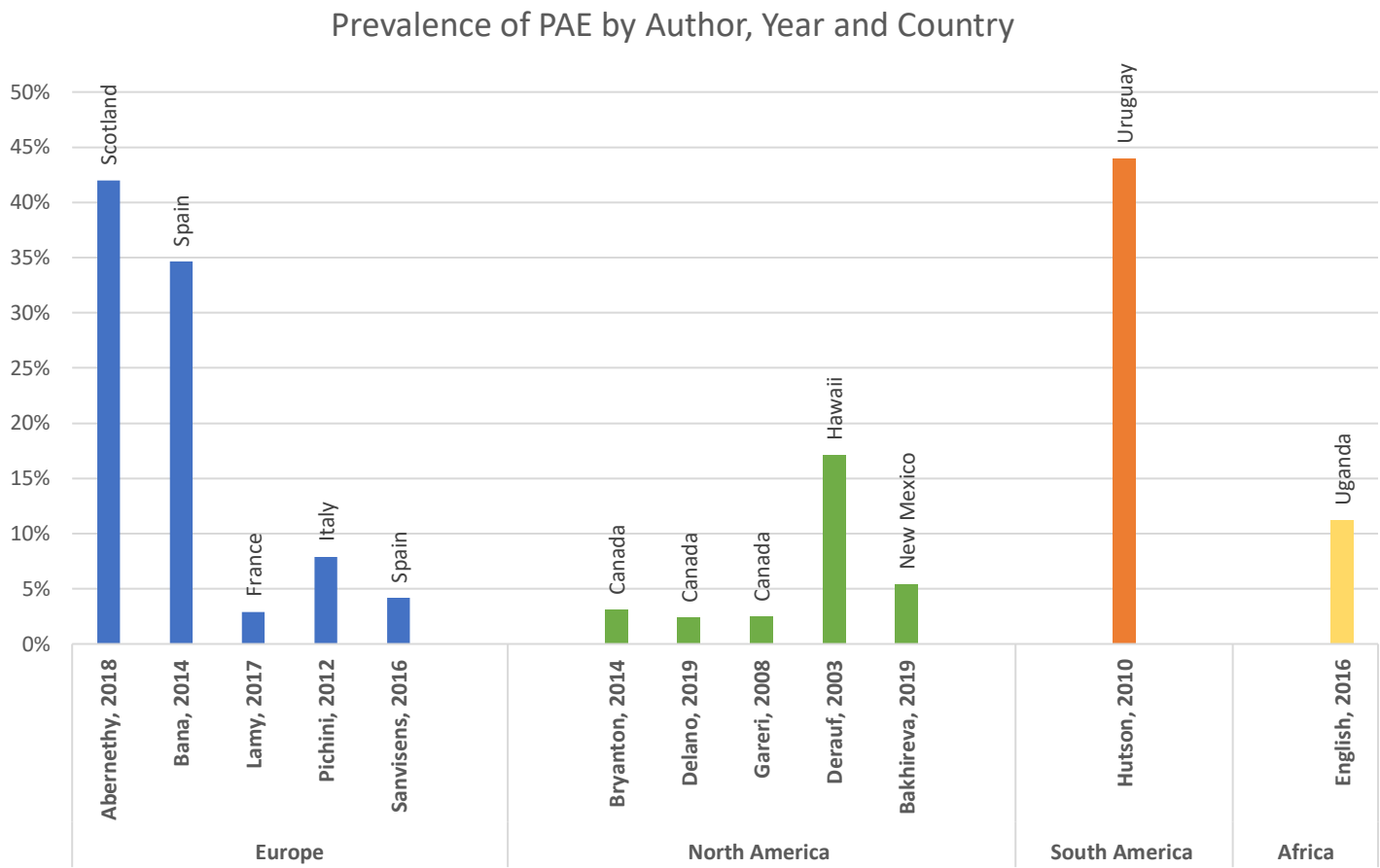
Four studies reported prevalence based on EtG and/or EtS analysis, although these also differed in the cut-off points used. Only one study (Abernethy et al., 2018) used the recommended cut-off of 30ng/g, whilst the other three used more conservative cut-offs of >40 ng/g (Lamy et al., 2017), >50 ng/g (Bana et al., 2014) and >274 ng/g (Sanvisens et al., 2016). Additionally, while the majority of studies reported prevalence as per individual biomarker and cut-off point, three studies did not and reported prevalence as indicated by either a positive result of ≥ 2 biomarkers (Bakhireva et al., 2019), or a summation of biomarkers (Bana et al., 2014; Sanvisens et al., 2016).

Overall, the prevalence of PAE as indicated by FAEE biomarkers in meconium ranged from 2.4% (Delano et al., 2019) to 44% (Hutson et al., 2010). Rates based on EtG results ranged from 2.9% (Lamy et al., 2017) to 15% (Abernethy et al., 2018), and EtS prevalence rates were

between 7.8% (Bakhireva et al., 2019) and 16.7% (Sanvisens et al., 2016). When investigated by geographical region, the highest rate was observed in Uruguay at 44% (Hutson et al., 2010), followed by Scotland at 42% (Abernethy et al., 2018). Rates in Spain were as low as 4.2% in one study (Sanvisens et al., 2016) and as high as 34.6% in another (Bana et al., 2014), despite cut-off points being much higher in the latter study (FAEE >1000ng/g/ and EtG >50 ng/g vs EtG ≥274 ng/g, EtS ≥ 1.51 ng/g). This is visually illustrated in Figure 3.

Figure 3

Bar Chart Depicting the Prevalence of PAE Based on Author, Year and Country as Determined by Meconium Biomarkers



Self-report prenatal alcohol use

All studies with the exception of Bryanton et al. (2014) collected information on self-reported PAU (illustrated in Table 5). Descriptive analysis of these results was explored, as well as the comparison of prevalence rates of self-reported PAU and meconium biomarkers

analysis in the studies which assessed this. However, results should be interpreted with caution as included studies are not representative of all studies utilising self-report methodology.

Prevalence rates based on self-report data ranged from 0.5% in Ontario, Canada (Gareri et al., 2008) to 37% in Uruguay (Hutson et al., 2010). Timing of reported alcohol consumption differed from "risky' alcohol consumption 12 months prior to pregnancy (Bakhireva et al., 2019) to 3rd trimester drinking (Lamy et al., 2017), and 'any' use throughout pregnancy duration (English et al., 2016). Collection and analysis of this data also varied greatly, as studies used different methods including questionnaires (Abernethy et al., 2018; Bana et al., 2014; Bryanton et al., 2014; Gareri et al., 2008; Hutson et al., 2010; Sanvisens et al., 2016), semi-structured interviews (Lamy et al., 2017), and validated alcohol screening measures including the AUDIT (Pichini et al., 2012), AUDIT-C (Bakhireva et al., 2019), TWEAK (English et al., 2016) and CAGE (Hutson et al., 2010). Half of the studies conducted analysis on comparability/level of agreement between self-reported PAU and PAE as obtained via meconium biomarkers. Four of these found that there was no agreement between self-reported PAU and detection of positive biomarkers in meconium (Derauf et al., 2003; Delano et al., 2019; English et al., 2016; Pichini et al., 2012), whilst two found poor levels of agreement as demonstrated by Kappa values of 0.06 (Hutson et al., 2010) and 0.13 (Lamy et al., 2017).

Overall, prevalence rates obtained via meconium testing were higher than self-reported PAU amongst the same sample in six of the eleven studies (Abernethy et al., 2018; Bana et al., 2014; Derauf et al., 2003; Gareri et al., 2008; Hutson et al., 2010; Sanvisens et al., 2016). Biomarker determined rates ranged from 1.2 times higher (in Uruguay; Hutson et al., 2010) to 14 times higher (in Scotland; Abernethy et al., 2018) than those obtained by maternal self-report methods.

Table 5

Study Results Table Reporting Prevalence of PAU using Meconium Testing & Maternal Self-reports

Study	Biomarker(s)	Cumulative cut-points	Analysis	No. of specimens analysed	Prevalence estimates %	Sample size	Prevalence of self-report PAU	Measure of self-report PAU	Level of agreement
Abernethy	FAEEs, EtG	FAEE > 600ng/g, EtG > 30ng/g	LC-MS/MS	235	42% (FAEEs), 15% (EtG)	325	3%	Informal questionnaire	-
Bakhireva	FAEEs, EtG, EtS	Ethyl laurate (>LOQ: 50 ng/g), ethyl myristate (> LOQ: 250 ng/g), ethyl palmitate (> LOQ: 50 ng/g), ethyl palmitoleate (> LOQ: 15 ng/g), ethyl stearate (> LOQ: 50 ng/g), ethyl oleate (> LOQ: 15 ng/g), ethyl linoleate (> LOQ: 15 ng/g), ethyl linolenate (> LOQ: 25 ng/g), and ethyl arachidonate (> LOQ: 15 ng/g). EtG >LOQ: 3.ng/g, EtS > LOQ: 5.0ng/g. *	LC-MS/MS	333	7.8% (EtS), 5.1% (EtG); 5.4% positive for ≥2 biomarkers	289	12.5% for "risky" alcohol use in the 12 months before enrolment	AUDIT-C questionnaire	-
Bana	FAEEs, EtG	FAEE >1000 ng/g, EtG > 50 ng/g	GC/MS & LC-MS/MS	101	34.65%; 17% positive for both	110	4.50%	Questionnaire	-
Bryanton	FAEEs	FAEE ≥ 2.00 nmol/g	GC/MS	1271	3.1% (for samples collected within 24h) (range 3.1-4.4%)	-	-	-	-
Delano	FAEEs	FAEE ≥ 2 nmol/g	SPME GC-MS	1315	2.4%	1315	32% "social level" drinking during pregnancy	-	No agreement

Derauf	FAEEs	FAEE ≥ 50 ng/g	GC/MS	422	17.10%	436	5.30%	Questionnaire	No agreement (k = –0.02, 95%CI: –0.04, 0.00)
English	FAEEs	FAEE > 2 nmol/g	GC/MS	503	11.2 %	505	16% "any" use during pregnancy, 3.2% "consistent use", 6.3% ''heavy consumption'' during any trimester. TWEAK results: Of n= 81 who reported PAU, 53% scored ≥2 points (possible problem drinking)	Standardised questionnaire & TWEAK	No agreement (p = 0.118)
Gareri	FAEEs	FAEE ≥ 2.00 nmol/g.	GC/MS	682	2.50%	1019	0.50%	Questionnaire	-
Hutson	FAEEs	FAEE > 2.00 nmol/g	GC/MS	824	44%	900	37% questionnaire; 14% CAGE questionnaire	Questionnaire % CAGE questionnaire	Poor agreement (k = 0.06; 95% CI: –0.02 to 0.14)
Lamy	EtG	EtG > 40 ng/g	GC/MS	642	2.9% (EtG)	724	3.7% during 3rd trimester	Semi-structured interview	Poor agreement (k = 0.13; 95%CI: 0.04-0.22)
Pichini	FAEEs, EtG, EtS	FAEE & EtG ≥ 2 nmol⁄g	LC/MS/MS	607	7.9% (0% in Verona, 4.0% in San Daniele del Friuli, 4.9% in Naples, 5.0% in Florence, 6.2% in Crotone, up to 10.6% in Reggio Emilia, and 29.4% in Rome)	607	28.9%	AUDIT questionnaire	No agreement
Sanvisens	EtG, EtS	EtG ≥274 ng/g, EtS ≥ 1.51 ng/g	LC-MS/MS	48	4.2% (EtG), 16.7% (EtS)	51	6%	Structured questionnaire	-

Note. * Authors deemed prevalence of PAU as % of population that were positive for ≥ biomarkers

Discussion

Overview

This review investigated the prevalence of PAE as obtained using meconium biomarkers of alcohol. Following a comprehensive systematic search of the literature, twelve studies reporting the prevalence of PAE using meconium biomarkers were identified and their methodological quality assessed. The review initially proposed to estimate a global pooled prevalence of PAE and identify prevalence rates by geographical location of the studies. This was not viable however due to the heterogeneity observed across studies with regards to large variation across methodology and analysis.

Interestingly, prevalence rates varied widely across the twelve studies. The lowest prevalence rate of PAE from meconium testing reported was 2.4% (Delano et al., 2019) and the highest rate 44% (Hutson et al., 2010). The former, a Canadian birth cohort study, recruited 2,000 volunteering women, the majority of whom were married (95%) and earning a gross annual income of over $80,000. The latter was a cross-sectional study conducted in Uruguay in a low socioeconomic sample of women; 18% of whom were married and 95% of whom had completed less than secondary level education. Similarly, a high prevalence rate of 42% was observed in a study recruiting from an inner-city maternity unit in Glasgow, Scotland (Abernethy et al., 2018). These results taken as a whole reflect findings from US literature, as higher risks of drinking have been observed amongst unmarried women, and more specifically, higher risk of 3rd trimester drinking amongst lower income groups (Shmulewitz & Hasin, 2019).

These studies are from different continents however, and this must be acknowledged in addition to the many other sociodemographic factors at play. A common misconception is that PAU is associated with poverty, and although Abernethy et al. (2018) demonstrated a high prevalence of PAU in their sample, which was predominantly of lower SES, they also found with subgroup analysis that positive meconium results were more common in women living in more affluent areas. Studies have demonstrated that women of higher SES report more frequent PAU than those of lower SES, while rates of FASD are higher in lower SES cohorts, possibly due to heavier consumption or binge drinking (May & Gossage, 2011; Shmulewitz & Hasin, 2019). Increased rates of inadequate prenatal care and social complexities are also factors related to higher rates of FASD (Singal et al., 2019), which are more prevalent in lower SES

groups. Regarding marital status, one possible explanation for higher rates of PAU in unmarried women may be lack of social support, which has been found to be a protective factor for reducing alcohol use in women (Leonardson & Loudenburg, 2007). Nonetheless, this highlights some of the many factors associated with PAU, which must be considered when interpreting prevalence rates.

Measurement of PAU also plays a role. A previous systematic review found that prevalence estimates based on meconium biomarkers were on average four times higher than those obtained using self-reports (Lange et al., 2014). In this review, 11 studies provided information on self-reported PAU, however only six of these indicated higher prevalence rates from meconium testing. Within these six studies, positive meconium results ranged from 1.2 to 14 times higher than self-reported rates of PAU. With regards to the other five studies, self-reported rates were higher than positive meconium biomarker rates, however this might be explained by the manner in which self-report data was collected. For example, Bakhireva et al. (2019) reported alcohol consumption in the 12 months prior to enrolment to the study, thus capturing consumption during pre-pregnancy and pregnancy stages. Additionally, Delano et al., 2019 found self-reported prevalence to be 13 times higher than the rate of positive meconium biomarkers (32% of social level drinking versus 2.4%). This 'social drinking level' equated to less that 2 standard drinks per week however, and only 0.2% of women reported drinking above this level, a rate tenfold lower than that found by meconium FAEE analysis. These highlight the limitations of self-report, particularly in detecting heavier alcohol consumption which objective measures appear to be more sensitive to.

Irrespective of the means of measurement, the global prevalence of PAU has been estimated at 10% (Popova et al., 2017), however half of the studies in this review had rates below this. Comparison of prevalence rates of alcohol use and alcohol exposure is complicated by a multitude of factors however, one being the methodology utilised to ascertain the data. As meconium testing typically reflects moderate to heavy exposure to alcohol during the later stages of pregnancy, women who drink modest amounts earlier on might not be detected. Conversely, this increases the possibility of false negative errors, represents missed opportunities to adequately support individuals with PAE and their families (Gifford & Bearer, 2015) and to possibly ameliorate effects of PAE by implementing neurodevelopmental interventions (Wozniak et al., 2020). Some authors have therefore suggested that self-report

measures are more effective at detecting lower PAE than objective measures despite likely underreporting (McQuire et al., 2016).

Strengths & limitations

The current review is the first of its kind and has several notable strengths, including the extensive search strategy, rigorous critical appraisal and application of stringent inclusion and exclusion criteria. Overall, the methodological quality of included studies was satisfactory. All studies were recruited from general maternity or antenatal settings, thus increasing the applicability of findings to general population samples in each respective geographical location. The majority of studies had adequate sample sizes for assessing prevalence rates (80%). Furthermore, 11 studies had recruited appropriately through either random or consecutive sampling, thereby increasing generalisability of results.

This review is not without its limitations, however. One significant shortcoming observed across the studies was the heterogeneity of analysis and methods employed. Only six studies used internationally accepted cumulative cut-off points for FAEE analysis and one for EtG analysis. Additionally, Lamy et al. (2017) found a high rate of false negative results from EtG biomarker analyses, further demonstrating the need to approach results of such tests with caution. In support of these findings were conclusions drawn from a meta-analysis conducted by McQuire et al. (2016). Authors found a lack of consensus across the levels of acceptability for diagnostic accuracy of biomarkers and high rates of false positive and false negative tests.

Although FAEE, EtG & EtS are validated biomarkers of PAE, there is no standardised quantification criteria for their analysis. In this review, some authors specified the FAEE's cumulated for analysis of prevalence rates, whilst others did not provide this information. Other studies reported prevalence based on the analysis of two positive biomarkers instead of one. Cut-off points for each biomarker also differed, with FAEE cut-off points ranging from 600 ng/g to 1000 ng/g, and EtG from 30 ng/g to 50 ng/g. There is lack of consensus regarding cut-off points for biomarkers, with some studies proposing that cut-off concentrations for FAEE's should be 10,000 ng/g (approx. 33 nmol/g) and others ranging from 200 ng/g to 600 ng/g (Delano et al., 2019). Consequently, sensitivity and specificity rates of these cut-offs vary considerably between 52%-100% and 43.1% to 98.4% respectively (Chan et al., 2004; Himes et al., 2015), although are highest with a cumulative cut-off of 2.0 nmol/g (Chan et al., 2003).

As a result, pooling estimates of prevalence rates is difficult across studies that appear homogenous in terms of recruitment and design but differ in their procedures and statistical analysis.

Limitations of review

Application of the eligibility criteria identified 12 studies for inclusion in this review, a reasonably small number given that research investigating the prevalence of PAE via meconium biomarkers began in the 1990's (Bearer et al., 1996; Mac et al., 1994; Niemelä et al., 1991). Furthermore, this review only included studies conducted in general maternity populations. In choosing to review the prevalence of PAU in general populations, the relevance of these findings to high-risk neonatal populations such as in Chan et al. (2004) is limited. Nonetheless, piloting of the search strategy and independent screening and assessment of quality by two reviewers permits confidence that the conclusions drawn from this systematic review are based on the synthesis of all available evidence in the area.

Generalisability

The heterogeneity of studies limits the ability to determine overall prevalence and to draw comparisons between countries. Recruitment methods varied, as well as procedures around the collection, storage and analysis of samples. Given the requirement for consent or voluntary nature of most studies, it is possible that some women who had consumed alcohol during pregnancy choose not to consent to the study or to provide meconium sample for analysis. These may have led to conservative prevalence rates and jeopardised the generalisability of findings.

Despite the above, findings reflect the diversity of the literature with respect to the varying levels of PAU observed across populations and geographical locations. It highlights the importance of collecting detailed maternal information in order to determine differences in prevalence between subgroups and explore the impact of sociodemographic factors on prevalence of PAU. Findings of each study in isolation can be utilised as per country and may be helpful in determining the risks of PAE within certain populations and regions so that universal screening strategies can be implemented. The discordance between rates of self-reported PAU and PAE as determined by meconium biomarkers further emphasizes the need for caution when interpreting results, but also raises the question as to whether objective

measures should be utilised in conjunction with subjective measures in order to better detect PAE at various stages throughout pregnancy. Objective measures may increase the accuracy of figures derived from self-report.

Implications

The current review demonstrates the sparsity of methodologically robust prevalence studies using meconium biomarkers and highlights an ongoing need for further research and clinical recommendations in antenatal care settings regarding the utility of meconium biomarkers. Alcohol consumption in pregnancy is a highly emotive topic and screening programmes need to be accurate and acceptable to the population. The WHO proposes that parameters for screening programmes must be set based on best evidence, cost-efficacy and feasibility (WHO, 2020). Evidently, more research is required to establish reliable and concrete evidence for objective measures, and to assess the most feasible methods for individuals, clinicians and stakeholders (McQuire et al., 2016). Further studies should explore the correlation of self-report measures with FAEE and EtG concentrations and should ensure they are utilising internationally recommended cut-off points. Methodological rigour is crucial in order to provide more reliable evidence regarding the clinical and scientific use of biomarkers and to allow for comparison across studies. Enhancing the accuracy of prevalence data on PAE would have far-reaching effects on the assessment and diagnoses of FASD, as it would help to facilitate assessment of risk and implementation of timely interventions.

This review included studies examining FAEE, EtG and EtS in meconium. There is a paucity of research on EtS, and only three of the studies in this review utilised this measure. Thus, conclusions drawn on the basis of EtS analysis are limited, and the evidence for its value in detection of PAU requires further research. Thresholds also need further consideration and more testing in general antenatal settings is required. The 2nmol/g cut-off for FAEEs is based on a study comparing women with alcohol problems to abstainers (Chan et al., 2003), and this raises a query as to whether it is appropriate for use in general populations. Recommendations for consistent and specific guidelines on the analysis of meconium biomarkers should be a focus of future research and policy makers.

As mentioned, meconium is produced in second and third trimesters and therefore positive biomarkers indicate PAU during these later stages of pregnancy. Meconium FAEE's

are limited in their ability to detect infrequent, but potentially harmful consumption during earlier stages (Bryanton et al., 2014). Thus, utilising such measures is likely to miss a proportion of women who have consumed alcohol in earlier stages but ceased during the course of the pregnancy or following recognition. Self-report methods may be more effective to capture this pattern of consumption, however, are vulnerable to recall and reporting bias and this may lead to underestimation of prevalence rates of PAU. Future research should ensure standardised self-report measures are employed which are appropriate for assessing PAU in general and non-high-risk pregnant populations. The AUDIT-C (Bush et al., 1998) has been validated in antenatal settings (Scottish Intercollegiate Guidelines Network [SIGN], 2019).

Currently diagnoses of FASD remains a challenge as the most common method employed to obtain information regarding PAU is self-report. Due to factors such as stigma and shame, it is unlikely that studies relying on maternal self-report alone can accurately estimate the prevalence of either PAE or FASD. If infants are not identified as at risk of FASD, appropriate screening and interventions cannot be implemented. This creates a perpetuating problem across the globe as individuals likely to be affected lack access to necessary provisions, which in turn result in more adverse outcomes. Improving methods used to obtain data on PAU would have far-reaching effects on diagnostic services, implementations for public health policies and recommendations for public health. Prevalence rates based on objective measures within general population samples are likely to be a closer true estimate of PAE.

Lastly, results of this review highlight the need to consider the links between social determinants of health and FASD. The evidence is clear that the direct cause of FASD is PAE, however drinking behaviour is affected by a multitude of social, economic and cultural factors such as poverty, genetics, adverse life events and poor social support systems around the individual (Jonsson et al., 2014). These need to be considered in the context of FASD, and in this review, higher rates of PAE as indicated by meconium were observed in lower socioeconomic status groups. Differentiating between higher-risk and lower-risk community samples is important both in the research conducted in this area and in the implementation of prevention strategies in order to improve efficacy and ensure acceptability of such interventions amongst different cohorts. These factors, as well as the inconsistent methodologies employed within research to assess prevalence of FASD suggest that a high degree of caution is required when interpreting results of prevalence studies as these can have significant impacts on the

public health advice given to women. The literature on the best practices for screening of PAE is limited, as also observed in this review, and these further highlight some of the ethical challenges associated with use of meconium biomarkers for screening PAE. Results indicate the need to consider these ethical implications, and more broadly, the need to approach the research with sensitivity and caution.

Conclusion

This review found that the prevalence of PAE as detected using meconium biomarkers varied widely across the literature, ranging from 2.4% to 44%. Significant variation amongst study methodologies precluded the utility of establishing a pooled prevalence of PAU. Nonetheless, the review highlighted the diversity of prevalence rates across maternal populations in different countries and provides support for the need for public health initiatives to direct attention towards PAE. Alcohol consumption during pregnancy is a growing public health issue, however capturing true prevalence rates remains a challenging feat. Gaining accurate estimates of the prevalence of PAU is vital for the assessment of potential risk, early diagnosis of FASD and access to adequate services. The implementation of appropriate screening programmes is a pivotal part of any primary prevention and early intervention approach for FASD. This review concludes that meconium biomarkers of PAE hold promise as an objective and valuable method, in comparison to self-report or questionnaires. However further research is required on its validity and acceptability to population-based samples in order to best inform screening strategies for use in routine clinical practice.

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Appendices

Appendix A Guidance for publication in BMC Pregnancy & Childbirth Journal

Retrieved from https://bmcpregnancychildbirth.biomedcentral.com/submission-guidelines/preparing-your-manuscript/review

Aims & Scope

BMC Pregnancy & Childbirth is an open access, peer-reviewed journal that considers articles on all aspects of pregnancy and childbirth. The journal welcomes submissions on the biomedical aspects of pregnancy, breastfeeding, labor, maternal health, maternity care, trends and sociological aspects of pregnancy and childbirth.

Review Criteria

Reviews are summaries of recent insights in specific research areas within the scope of *BMC Pregnancy and Childbirth*. Key aims of Reviews are to provide systematic and substantial coverage of a research or clinical area of wide interest or to present a critical assessment of a specified area. A review must focus on recent research and on a topic that is timely and relevant to the field. All Reviews published by *BMC Pregnancy and Childbirth* are peer-reviewed. Most Reviews are commissioned by the Editor of *BMC Pregnancy and Childbirth* and we do not encourage unsolicited submissions for this type of article. Review articles may be considered at the Editor's discretion and their decision on consideration is considered final.

Preparing your manuscript

The information below details the section headings that you should include in your manuscript and what information should be within each section.Please note that your manuscript must include a 'Declarations' section including all of the subheadings (please see below for more information).

Title page: The title page should: present a title that includes, if appropriate, the study design e.g.: "A versus B in the treatment of C: a randomized controlled trial", "X is a risk factor for Y: a case control study", "What is the impact of factor X on subject Y: A systematic review" or for non-clinical or non-research studies: a description of what the article reports list the full names and institutional addresses for all authors if a collaboration group should be listed as an author, please list the Group name as an author. If you would like the names of the individual members of the Group to be searchable through their individual PubMed records, please include this information in the "Acknowledgements" section in accordance with the instructions below indicate the corresponding author.

Abstract: The Abstract should not exceed 350 words. Please minimize the use of abbreviations and do not cite references in the abstract.

Keywords: Three to ten keywords representing the main content of the article.

Background: The Background section should explain the background to the article, its aims, a summary of a search of the existing literature and the issue under discussion.

Main text: This should contain the body of the article, and may also be broken into subsections with short, informative headings.

Conclusions: This should state clearly the main conclusions and include an explanation of their relevance or importance to the field.

List of abbreviations: If abbreviations are used in the text they should be defined in the text at first use, and a list of abbreviations should be provided.

Declarations: All manuscripts must contain the following sections under the heading 'Declarations':Ethics approval and consent to participate, Consent for publication, Availability of data and materials, Competing interests, Funding, Authors' contributions, Acknowledgements, Authors' information (optional)

Please see below for details on the information to be included in these sections. If any of the sections are not relevant to your manuscript, please include the heading and write 'Not applicable' for that section.

Ethics approval and consent to participate: Manuscripts reporting studies involving human participants, human data or human tissue must:include a statement on ethics approval and consent (even where the need for approval was waived)& include the name of the ethics committee that approved the study and the committee's reference number if appropriate

Studies involving animals must include a statement on ethics approval and for experimental studies involving client-owned animals, authors must also include a statement on informed consent from the client or owner. See our editorial policies for more information. If your manuscript does not report on or involve the use of any animal or human data or tissue, please state "Not applicable" in this section.

Consent for publication: If your manuscript contains any individual person's data in any form (including any individual details, images or videos), consent for publication must be obtained from that person, or in the case of children, their parent or legal guardian. All presentations of case reports must have consent for publication.You can use your institutional consent form or our consent form if you prefer. You should not send the form to us on submission, but we may request to see a copy at any stage (including after publication). See our editorial policies for more information on consent for publication. If your manuscript does not contain data from any individual person, please state "Not applicable" in this section.

Availability of data and materials. All manuscripts must include an 'Availability of data and materials' statement. Data availability statements should include information on where data supporting the results reported in the article can be found including, where applicable, hyperlinks to publicly archived datasets analysed or generated during the study. By data we mean the minimal dataset that would be necessary to interpret, replicate and build upon the findings reported in the article. We recognise it is not always possible to share research data publicly, for instance when individual privacy could be compromised, and in such instances data availability should still be stated in the manuscript along with any conditions for access.

Data availability statements can take one of the following forms (or a combination of more than one if required for multiple datasets):

- The datasets generated and/or analysed during the current study are available in the [NAME] repository, [PERSISTENT WEB LINK TO DATASETS]
- The datasets used and/or analysed during the current study are available from the corresponding author on reasonable request.
- All data generated or analysed during this study are included in this published article [and its supplementary information files].
- The datasets generated and/or analysed during the current study are not publicly available due [REASON WHY DATA ARE NOT PUBLIC] but are available from the corresponding author on reasonable request.
- Data sharing is not applicable to this article as no datasets were generated or analysed during the current study.
- The data that support the findings of this study are available from [third party name] but restrictions apply to the availability of these data, which were used under license for the current study, and so are not publicly available. Data are however available from the authors upon reasonable request and with permission of [third party name].
- Not applicable. If your manuscript does not contain any data, please state 'Not applicable' in this section.

More examples of template data availability statements, which include examples of openly available and restricted access datasets, are available here. BioMed Central also requires that authors cite any publicly available data on which the conclusions of the paper rely in the manuscript. Data citations should include a persistent identifier (such as a DOI) and should ideally be included in the reference list. Citations of datasets, when they appear in the reference list, should include the minimum information recommended by DataCite

and follow journal style. Dataset identifiers including DOIs should be expressed as full URLs. For example: Hao Z, AghaKouchak A, Nakhjiri N, Farahmand A. Global integrated drought monitoring and prediction system (GIDMaPS) data sets. figshare. 2014. http://dx.doi.org/10.6084/m9.figshare.853801. With the corresponding text in the Availability of data and materials statement: The datasets generated during and/or analysed during the current study are available in the [NAME] repository, [PERSISTENT WEB LINK TO DATASETS].[Reference number] If you wish to co-submit a data note describing your data to be published in *BMC Research Notes*, you can do so by visiting our submission portal. Data notes support open data and help authors to comply with funder policies on data sharing. Co-published data notes will be linked to the research article the data support (example).

Competing interests: All financial and non-financial competing interests must be declared in this section. See our editorial policies for a full explanation of competing interests. If you are unsure whether you or any of your co-authors have a competing interest please contact the editorial office. Please use the authors initials to refer to each authors' competing interests in this section. If you do not have any competing interests, please state "The authors declare that they have no competing interests" in this section.

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Authors' contributions: The individual contributions of authors to the manuscript should be specified in this section. Guidance and criteria for authorship can be found in our editorial policies. Please use initials to refer to each author's contribution in this section, for example: "FC analyzed and interpreted the patient data regarding the hematological disease and the transplant. RH performed the histological examination of the kidney, and was a major contributor in writing the manuscript. All authors read and approved the final manuscript."

Acknowledgements: Please acknowledge anyone who contributed towards the article who does not meet the criteria for authorship including anyone who provided professional writing services or materials. Authors should obtain permission to acknowledge from all those mentioned in the Acknowledgements section.See our editorial policies for a full explanation of acknowledgements and authorship criteria. If you do not have anyone to acknowledge, please write "Not applicable" in this section.

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Footnotes: Footnotes can be used to give additional information, which may include the citation of a reference included in the reference list. They should not consist solely of a reference citation, and they should never include the bibliographic details of a reference. They should also not contain any figures or tables. Footnotes to the text are numbered consecutively; those to tables should be indicated by superscript lower-case letters (or asterisks for significance values and other statistical data). Footnotes to the title or the authors of the article are not given reference symbols. Always use footnotes instead of endnotes.

Appendix B Search Syntax

Database	Syntax
Medline, Embase and PsycINFO	(prevalen* or epidemiolog* or frequenc* or occur* or inciden* or probability or rate* or statistic) AND (pregnan* or prenatal or pre natal or antenat* or postnat* or primigravida or expect* mother* or expect* mum* or matern* or maternal-fetal exchange or newborn* or baby or Infant) AND (Alcohol* or binge drinking or ARBD or ARND or drunk* or ethanol or FAS or FASD or Intoxicat* or PAE or pFAS) AND (meconium or FAEE or "alcohol metabolite*" or "fatty acid* ethyl or ester*" or etg or "ethyl glucuronide*" or ets or "ethyl sulfate*")
Proquest dissertations and Thesis Global	Meconium OR prevalence OR prenatal OR alcohol OR pregnan*
CINAHL Plus	(prevalen* or epidemiolog* or frequenc* or occur* or inciden* or probability or rate* or statistic) AND (pregnan* or prenatal or pre natal or antenat* or postnat* or primigravida or expect* mother* or expect* mum* or matern* or maternal-fetal exchange or newborn* or baby or Infant) AND (Alcohol* or binge drinking or ARBD or ARND or drunk* or ethanol or FAS or FASD or Intoxicat* or PAE or pFAS) AND (meconium or FAEE or "alcohol metabolite*" or "fatty acid* ethyl or ester*" or etg or "ethyl glucuronide*" or ets or "ethyl sulfate*")
SCOPUS	(prevalen* or epidemiolog* or frequenc* or occur* or inciden* or probability or rate* or statistic) AND (pregnan* or prenatal or pre natal or antenat* or postnat* or primigravida or expect* mother* or expect* mum* or matern* or maternal-fetal exchange or newborn* or baby or Infant) AND (Alcohol* or binge drinking or ARBD or ARND or drunk* or ethanol or FAS or FASD or Intoxicat* or PAE or pFAS) AND (meconium or FAEE or "alcohol metabolite*" or "fatty acid* ethyl or ester*" or etg or "ethyl glucuronide*" or ets or "ethyl sulfate*")
OPENGREY	Meconium OR prevalence OR prenatal OR alcohol OR pregnan*

Appendix C Critical Appraisal Tool

JBI Critical Appraisal Checklist for Studies Reporting Prevalence Data

Reviewer_____Date_____

Author _____Year_____Record Number _____

	Yes	No	Unclear	Not applicable
1. Was the sample frame appropriate to address the target population?	☐	☐	☐	☐
2. Were study participants sampled in an appropriate way?	☐	☐	☐	☐
3. Was the sample size adequate?	☐	☐	☐	☐
4. Were the study subjects and the setting described in detail?	☐	☐	☐	☐
5. Was the data analysis conducted with sufficient coverage of the identified sample?	☐	☐	☐	☐
6. Were valid methods used for the identification of the condition?	☐	☐	☐	☐
7. Was the condition measured in a standard, reliable way for all participants?	☐	☐	☐	☐
8. Was there appropriate statistical analysis?	☐	☐	☐	☐
9. Was the response rate adequate, and if not, was the low response rate managed appropriately?	☐	☐	☐	☐

Overall appraisal: Include ☐ Exclude ☐ Seek further info ☐

Comments (Including reason for exclusion)

_____

_____

_____

Chapter 2: Empirical study

Prenatal alcohol use in the UK: A study exploring self-reported drinking during pregnancy and the impact of an educational intervention on knowledge and attitudes

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Abstract

Background: Prenatal alcohol consumption is a significant public health concern due to its teratogenic effects. Current WHO guidelines recommend that women should abstain from alcohol throughout their pregnancy, although prevalence rates remain high. This study explores the self-reported prevalence of prenatal alcohol use of pregnant, or recently pregnant, women in the UK and the impact of an educational intervention on attitudes and knowledge towards drinking during pregnancy.

Methods: A national cross-sectional study recruited 1,536 women in the UK aged 19 to 50 years (M = 33.3 years, SD = 4.89), from July 2020 to December 2020. An anonymous online questionnaire comprising an educational intervention and measures assessing prevalence, attitudes and knowledge was administered.

Results: High rates of binge drinking were observed prior to pregnancy (82%), although decreased significantly following recognition of pregnancy (0.2%). One quarter of women reported drinking during pregnancy following recognition, and almost one in five women had not heard of the term FASD. The educational intervention had a significant impact (z = -9.67, $p < .001$ r = 0.29), and led to more negative attitudes towards prenatal alcohol use and improved knowledge of the associated risks. Level of education and pre-existing attitudes were predictive of greater improvement [F (12, 1047) = 25.838, $p < .001$, adj. R^2 = .22].

Conclusions: This study is the first of its kind to explore self-reported prevalence of prenatal alcohol use in the UK via an anonymous online survey, and the impact of an educational intervention on attitudes and knowledge. Findings support the utility of education interventions in improving knowledge of risks and increasing negative attitudes towards drinking during pregnancy. Implementation of such interventions at community and clinical levels is recommended to reduce prenatal alcohol consumption and subsequently, the prevalence of FASD.

Keywords: Pregnancy; Alcohol; Attitudes towards drinking; Knowledge; Educational intervention

Introduction

Women, alcohol, and pregnancy

Alcohol consumption has increased globally, and the highest levels are observed in the WHO European Region (World Health Organisation, 2018). Women's level of consumption in particular has risen steadily alongside cultural shifts in gender roles, increasing gender equality, and changes in attitudes towards drinking (Slade et al., 2016). Consumption during pregnancy, otherwise known as prenatal alcohol use (PAU), is a significant global health concern and the negative impacts of alcohol exposure in pregnancy are well established, including increased risks of miscarriage, preterm birth and foetal alcohol spectrum disorder (FASD). Global prevalence of PAU is estimated to be 9.8%, and the UK has the fourth highest estimated prevalence worldwide at 41.3% (Popova et al., 2017).

International guidelines on PAU and what constitutes 'safe' levels of drinking during pregnancy have changed over time, leading to inconsistent messages from public health bodies. Until relatively recently, UK guidelines recommended that women should abstain from drinking during the pre-conception phase and first trimester, but if they choose to drink while pregnant, they should limit consumption to 1-2 units, once or twice a week (National Institute for Health and Clinical Excellence [NICE], 2008). However, in April 2016, the UK's Chief Medical Officer's (CMO) guidelines changed and advised that, given the absence of robust evidence, a 'precautionary approach' should be taken, and women should abstain from alcohol both during the pre-conception phase and throughout their pregnancy (Department of Health, 2016). Current international guidelines echo this and recommend that pregnant women should abstain from alcohol consumption (Holland et al., 2016). This precautionary approach has sparked debate due to limited evidence surrounding the risks of low-level consumption.

Ascertaining accurate estimates of the prevalence of PAU is challenging, and consumption during early stages prior to confirmation of the pregnancy is likely to be underreported or undetected. This is problematic as the foetus during the first trimester is particularly vulnerable to harm caused by alcohol (Schölin, 2016). In a multi-centre cohort study of 5,628 primigravida women across the UK, Ireland, New Zealand and Australia, one quarter reported low level PAU throughout (3-7 units per week) and a further 23% reported binge drinking (6 or more units in one session) during the first 15 weeks of pregnancy (McCarthy et al., 2013). The majority of women reduced their consumption or abstained

completely following recognition, a trend observed across research (Cameron et al., 2013; McCormack et al., 2017; Tough et al., 2006). However, unplanned pregnancies need to be considered as these can inevitably result in higher risks of inadvertent exposure of alcohol to the foetus (Schölin, 2016). In England, 45% of births are unplanned (Public Health England, 2018).

The heterogeneity of studies adds further complexity to the interpretation of prevalence rates as methodologies differ greatly. Self-report measures are likely to underestimate the level of PAU due to reporting and recall bias, and social stigma. Objective measures such as meconium biomarkers have been demonstrated to be more accurate, however cannot detect first trimester exposure (Lange et al., 2014). Definitions on what constitutes light, moderate and heavy consumption vary considerably across studies (Stade et al., 2009), and measurements of standard units of alcohol differ by country and type of alcoholic beverage, making it difficult to compare epidemiological studies (Clark et al., 1999). To improve collection of data on PAU several screening questionnaires have been developed and validated for use in antenatal settings. These are supported by clinical guidance and include the TWEAK, T-ACE, and AUDIT-C (Scottish Intercollegiate Guidelines Network [SIGN], 2019)

Foetal alcohol spectrum disorder (FASD)

FASD is an umbrella term used to describe a range of features that can occur as a result of PAU including structural or functional CNS abnormalities, cognitive and neurobehavioral impairments, and sentinel facial features (SIGN, 2019). Individuals with FASD often have difficulties with language, memory, learning and behaviour, as well as physical impairments. These can have lifelong implications, and place significant burden on the individual, their family and society. The economic burden is also high, with one study estimating the costs to be approximately 1.8 billion Canadian dollars per year (Popova et al., 2016), a population just over half of the UK's. Due to the challenges associated with screening for PAU and subsequent diagnosis, the actual rate of FASD is unknown. A meta-analysis estimated FASD prevalence in the UK to be 32.4 per 1,000 population (Popova et al., 2017). Furthermore, a more recent population-based cohort study calculated a screening prevalence estimate of FASD in order to represent the proportion that would have retrospectively met criteria for FASD in the UK (McQuire et al., 2019). Authors evaluated data collected from 13,495 children born between 1991 and 1992 and found a prevalence estimate of up to 17%.

Identification of babies exposed to alcohol is crucial for early diagnosis and intervention, and the absence of such can manifest in secondary adverse outcomes. A longitudinal study conducted by Streissguth et al. (1996) found that 94% of individuals with foetal alcohol effects experienced mental health problems, 60% of those aged 12 and over experienced trouble with the law, 79% had employment problems and a further 83% required dependent living situations. Diagnosis is challenging however and can be complicated by the overlapping features of genetic and malformation syndromes which share similar clinical characteristics to FASD, thus requiring careful differential diagnosis (British Medical Association, 2016). The continuing lack of consensus about what is considered 'safe' levels of consumption can impact on screening and diagnosis as women may or not meet certain criteria for exposure.

Some studies have found evidence of harm with low level consumption and have demonstrated that PAU is associated with cognitive impairments in the areas of learning, attention, visuospatial memory, and cognitive flexibility (Burden et al., 2005; Jacobson & Jacobson, 2002; Streissguth, 2007). Others have argued that light to moderate drinking is not a risk factor for neurodevelopmental difficulties (Alati et al., 2008; Kelly et al., 2009; Kelly et al., 2013) or behavioural problems (Robinson et al., 2010). Nevertheless, a review of the literature concluded that that there is a narrow margin between levels of consumption before there is increased risk to the foetus and thereby supported guidelines advising abstinence (O'Leary & Bower, 2012).

Interventions

Numerous preventative approaches to reduce PAU and the incidence of FASD have been developed and implemented and can be classified into three categories. Universal prevention strategies aim to inform the general public of the risks associated with PAU and include public health interventions such as media campaigns and education interventions. Selective prevention strategies target women of reproductive age and populations at risk (e.g., women who drink during pregnancy) and include clinical interventions such as brief interventions (BI's) and motivational interviewing. Indicated prevention strategies target women who are at high risk (e.g., require referral to specialist alcohol services) and incorporate pharmacological interventions (Clarren et al., 2011).

Regarding more targeted approaches for high-risk pregnant populations, the evidence for utility of pharmacological interventions is limited, as indicated by a systematic review conducted by Smith et al. (2009). Psychosocial interventions may show more promise, and motivation enhancement therapy has demonstrated efficacy in reducing alcohol and drug use in pregnant women receiving substance use treatment (Osterman et al., 2017).

Selective and universal prevention strategies have received more attention in general pregnant populations, although the overall evidence for their use in antenatal settings is inconclusive. Reviews of randomised and non-randomised controlled trials have demonstrated support for their utility in improving knowledge and reducing PAU (Crawford-Williams et al., 2015) as well as increasing abstinence rates (Stade et al., 2009; Gilinsky et al., 2011; Ujhelyi Gomez et al., 2020), however they also report significant heterogeneity and a paucity of methodologically robust studies. These authors concluded there was some evidence to suggest that BI's are beneficial in supporting women to maintain abstinence during pregnancy. This was also demonstrated by O'Connor and Whaley (2007) who found that pregnant women that had undergone a BI were five times more likely to report abstinence, and their newborns more likely to have better outcomes when compared to a control group.

BI's have therefore been recommended as cost-effective preventative measures which can be practically delivered and have a robust evidence base, as demonstrated in an overview (O'Donnell et al., 2014). They involve an initial screening stage to identify hazardous drinking, and a time-limited structured conversation aimed to support the person to think about changing their drinking behaviours in order to reduce risk of harm (Scobie & Woodman 2017). Other techniques employed in brief educational and psychological interventions include motivational interviewing, education, goal setting, or assessment for alcohol dependency. Motivational interviewing interventions have also shown success in reducing the number of alcohol exposed pregnancies through lower PAU and more effective contraception use (Project CHOICES Intervention Research Group, 2003). BI and motivation interviewing based interventions are based on principles from social cognitive theory (Bandura, 1986), motivational enhancement (Miller & Rollnick, 2002), the transtheoretical model (Prochaska et al., 1993) and self-efficacy (Bandura, 1977).

Due to different techniques and theories underlying interventions, research has started to analyse interventions at a more fundamental level by investigating their 'active ingredients', known as behaviour change techniques (BCT's). A meta-analysis conducted by Ujhelyi Gomez and colleagues (2020) found that the most commonly employed BCT's in psychosocial interventions aimed at reducing PAU were information about health consequences, goal setting, social support, and action planning. These as well as behavioural contracts, problem solving, self-talk and assessing readiness to change have been found to be effective BCT's for decreasing alcohol consumption (Fergie et al., 2019).

Overall, the research illustrates large variability in the types of interventions delivered, making it difficult to determine those with the greatest efficacy. Brief educational and psychological interventions show most promise, and from an ethical perspective, are positive for the mother and the developing foetus. Furthermore, they are equitable, can be made easily accessible and delivered quickly, and generally have low implementation costs (Scobie & Woodman, 2017). Web-based interventions for individuals with alcohol use problems have also been on the rise over the past few years and offer a viable and cost-effective mode of delivery (Balhara & Verma, 2014). However, these have mainly been utilised in adolescent and student populations and have yet to be explored in pregnant populations. There is an apparent need for further research on interventions in antenatal settings in order to decrease PAU and incidence of FASD.

Knowledge of risk and attitudes

Provision of information on the risks associated with PAU and current guidelines may help to change attitudes and social norms around drinking (British Medical Association, 2016). This is supported by both general social marketing intervention research (Kubacki et al., 2015) and research demonstrating that universal interventions to raise awareness of PAU can impact on attitudes (Bazzo et al., 2015; Ihlen et al., 1993) and knowledge, thus having the potential to lower FASD prevalence (Chersich et al., 2012). Attitudes towards PAU and drinking behaviours during current and past pregnancies have been found to be the strongest predictors of PAU (Peadon et al., 2011; Peadon et al., 2010), however research is limited.

International guidelines recommend that all pregnant women are screened for alcohol use by healthcare professionals (WHO, 2014), however, eliciting this information is

challenging due to potential stigmatisation, the negative attitudes of others, and concerns regarding child protection (Burns et al., 2010). Pregnant women who consume alcohol fear they will be perceived negatively by the public and healthcare professionals (Bell et al., 2016), may be concerned about the possible harm to their baby and, are therefore dissuaded from disclosing this information (Jones et al., 2011; Muggli et al., 2015).

Knowledge also plays a role, and research has shown that many women do not understand risks of harm associated with PAU with 20% of women having a "tolerant" attitude towards it (Elliott, 2014). Qualitative research on women's perceptions of the information and advice given around PAU reports ongoing confusion around safe levels of consumption and inconsistent messages (Anderson et al., 2014; Latuskie et al., 2019), and changes to guidance over time is likely to have exacerbated this. Women's attitudes towards guidance can impact on their decision to consume alcohol. Holland et al. (2016) investigated women's perception of the public health advice recommending abstinence and found that whilst some viewed this as responsible, others condemned it as a way of policing women. Authors concluded that the women in the study felt it was generally acceptable to drink responsibly while pregnant and supported their views by normalising occasional drinking and emphasising lower levels of consumption with lower risks. Similar findings have been reported by several other studies (Elek et al., 2013; Kesmodel & Schiøler Kesmodel, 2002; Meurk et al., 2014).

From the perspective of healthcare professionals there can be a reluctance to ask or advise about PAU and, due to varying attitudes and level of knowledge of the guidelines and risks of PAU, different recommendations are often given to patients (Coons et al., 2017). Not all healthcare providers routinely discuss alcohol use with women of childbearing age (Tough et al., 2005), or use validated screening tools (Wangberg et al., 2015). Midwives may be knowledgeable about the associated risks of PAU but may not always adhere to guidelines and, may lack the confidence to advise women about PAU (Payne et al., 2014). Other barriers include competing priorities, time constraints, inadequate skills or protocol and the relationship between women and their healthcare provider (Oni et al., 2019). It is therefore not surprising that missed opportunities to identify PAU during the pre-conception phase and throughout pregnancy occur, and subsequently lead to underreporting of prevalence and underdiagnosis of FASD.

Rationale

PAU is a significant public health concern in the UK, and despite recommendations for abstinence, estimated rates remain high. A multitude of barriers exist when attempting to accurately obtain information about PAU, and doing this in a confidential, anonymous manner has been suggested in order to reduce reporting bias and support women in providing this information (Muggli et al., 2015). This study is the first of its kind in the UK to assess PAU in a large sample of self-selected women in such an anonymous manner.

Furthermore, knowledge and attitudes are important determinants of health behaviour, however there is limited research exploring the impact of interventions on these in the context of PAU. Research has typically used change in maternal drinking behaviours as a measure of efficacy of preventative interventions (Ospina et al., 2011). Additionally, studies have predominantly recruited women with either reported PAU or those at high risk of PAU (Stade et al., 2009; Gilinsky et al., 2011; Ujhelyi Gomez et al., 2020), thus lacking generalisability to the wider population. This study aims to address these gaps by assessing the efficacy of an information leaflet in changing attitudes and knowledge towards drinking in a sample of pregnant, or recently pregnant, women. By better understanding attitudes and knowledge of women towards drinking during pregnancy, recommendations for intervention research and clinical practice can be made.

Objectives and research questions

The following research questions were assessed:

1. What is the prevalence of self-reported PAU in a self-selected sample of women in the UK?
2. What are women in the UK's attitudes towards, and knowledge of, the risks of PAU?
3. Can an information leaflet have an impact on attitudes and knowledge towards PAU?
4. What factors predict change in attitude and knowledge following the intervention?

Method

This cross-sectional study implemented a quasi-experimental within-subjects pre and post-test design. An online self-administered anonymous questionnaire was developed and administered via Qualtrics, a web-based survey software programme (https://www.qualtrics.com/).

Participants

Inclusion criteria were women in the UK over the age of 18, who had been pregnant at any time since April 1st, 2016 or were pregnant at the time of participation (during the recruitment period July 20th, 2020 to December 31st, 2020). Participants had to be residing in the UK at the time of pregnancy and study completion and have sufficient English language literacy skills to complete the survey. Those who did not meet criteria or required additional support needs were excluded. The date of April 1st, 2016 was chosen as a cut-off point due to changes in policy and healthcare guidance on PAU in the UK. There was no restriction placed on whether it was the participants' first pregnancy, and participants were advised to report on their most recent pregnancy if they had had more than one since April 2016.

Procedure

Recruitment took place online via social media platforms such as Facebook, Twitter, and LinkedIn. The study was advertised via an online poster (Appendix F) and promoted on various sites on these platforms, for example Facebook "Mums" and "Mums-to-be" groups. Appropriate agencies and organisations such as Mumsnet, National Childbirth Trust, Maternal Mental Health Alliance and FASD Network UK were also informed of the study and could choose to share details with members/followers on their webpages, forums, and social media platforms. Emails with the poster were sent to the above organisations on a monthly basis during the recruitment phase, which provided a description of the study and invited those interested to take part by following an electronic link to the study on Qualtrics.

The Qualtrics link led first to the participant information sheet and then to the consent form. Following indication of consent, the participant was directed through the questionnaire, which was divided into various sections. The intervention i.e., an information leaflet was embedded in the questionnaire, and participants were instructed to read the leaflet (either in pdf form or on their web browser, dependent on their device) and following this return to the

questionnaire. On completion, a debrief page was provided and participants were informed that they could access a summary of the findings of the study on this webpage once completed in May 2021. The study was expected to take approximately 20 minutes and participants were given the option following the questionnaire to enter into a prize draw to win one of three £50 Amazon Gift Cards. If they chose to enter, they were directed to another Qualtrics link.

Ethical considerations

Ethical approval was obtained by the DClinPsychol Ethics Committee within the University of Edinburgh (illustrated in Appendix B). No identifiable participant information was obtained in the survey and in order to protect respondent anonymity, an 'Anonymous Link' hyperlink was utilised before distribution, disabling the survey from collecting participants' IP addresses. Details of the study and its voluntary nature were outlined in the participant information sheet and consent form (Appendices D & E).

All information collected was stored securely on the Qualtrics platform, which is GDPR compliant. Opt-in to the prize draw was facilitated via an anonymous hyperlink, which was stored separately and not linked to survey responses. Although participants were unlikely to be considered vulnerable or exposed to harm whilst undertaking the study, information and support services were detailed at numerous points and links were provided should they wish to seek further support. Participants were also informed they could withdraw from the study any time.

Measures

Demographic information

A bespoke questionnaire gathered information on participant's age, ethnicity, marital status, employment status, level of education, and mental health status. Information on pregnancy was also captured including year of pregnancy, location of residency at the time, whether it was a planned pregnancy, and at what stage the participant found out they were pregnant.

Alcohol Consumption

A screening question was utilised to ascertain whether the participant had ever previously consumed alcohol. Information on PAU was then captured using the Alcohol Use

Disorders Identification Test - Consumption (AUDIT-C; Bush et al., 1998), a 3-item screening tool for an estimation of alcohol consumption. This is a shortened version of the 10-item AUDIT measure (Saunders et al., 1993), validated for use in pregnant populations (Dawson et al., 2005) and recommended for guiding conversation on PAU (Murdoch Children's Research Institute, 2010). It has robust psychometric properties and has been shown to demonstrate high levels of sensitivity (95%) and specificity (85%) in pregnant women (Burns, et al., 2010).

AUDIT-C questions measure (1) the frequency of drinking, (2) the quantity of alcohol consumed on a typical day, and (3) the frequency of drinking ≥6 alcoholic drinks on one occasion. A total score is calculated to provide an indication of risks to the individual's health and used as a brief screen for alcohol problems.

The AUDIT-C was utilised twice; to capture levels of alcohol consumption prior to the participant finding out she was pregnant and following this during the pregnancy. For example, participants were asked: "Before you found out that you were pregnant, how often did you have a drink containing alcohol?" and "During your pregnancy, how often did you have a drink containing alcohol?".

A visual guide on what is one standard unit of alcohol (from www.drinkaware.co.uk) accompanied this measure. One further question asked if there had been a change in participants drinking habits after they found out they were pregnant.

Attitudes and knowledge

Attitudes and knowledge of PAU were assessed utilising a 12-item 'Alcohol and Pregnancy Questionnaire' (Peadon et al., 2011). This questionnaire was initially adapted from the Health Canada survey titled 'Alcohol Use During Pregnancy and Awareness of Fetal Alcohol Syndrome' which was utilised in a survey on 2724 Canadian women (Environics Research Group, 2006). Following modification and a pilot study, the measure was used in an Australian nationwide cross-sectional study of 1102 women aged between 18-45 years. To date, psychometric data on this measure has yet to be published, but it remains the only measure of attitudes and knowledge towards PAU. Participants responded to these items on a 5-point Likert scale (from 1, *Strongly agree,* to 5, *Strongly disagree).*

Additional items on knowledge of FASD and awareness of risks associated with PAU were also obtained from Peadon et al.'s (2011) study. Participants were asked to rate 7 items on a 5-point scale whether they thought drinking during pregnancy increased certain risks such as miscarriage or seizures. One question asking whether participants had heard of the term FASD was also included.

Guidance on prenatal alcohol consumption

Guidelines and recommendations from the UK's CMO regarding alcohol consumption during pregnancy were extracted from the Department of Health's 'Alcohol Guidelines Review' (2016). Awareness and attitudes towards these were ascertained by 4 questions designed by the research team. For example, participants were asked if they were aware of the guidance, how much they agreed with aspects of it on a 5-point Likert scale (from 1, *Strongly agree,* to 5, *Strongly disagree),* and if they felt the message was widely known throughout the UK.

Intervention

The intervention comprised of an information leaflet known as 'Alcohol and pregnancy', developed by the Royal College of Obstetricians and Gynaecologists (2018). The information in this outlined the effects of prenatal alcohol consumption on a baby's development in the womb and gave information about FASD and guidance on alcohol consumption during pregnancy (illustrated in Appendix G).

Power calculation

G* Power was used a priori to guide sample size calculations for pre and post analysis and multiple regression (Faul et al., 2007). A two-tailed approached with a medium effect size (d = 0.5) and alpha level of 0.05 indicated that a sample size of 57 would be required to detect differences using Wilcoxon signed-rank test. The minimum sample size for a multiple regression with 6 predictor variables, an alpha level of 0.05 and moderate effect size (f^2= 0.15) was 146.

As an objective of this study was to assess self-reported prevalence of PAU in the UK, prevalence data was also used to guide sample size calculations. Previous research has estimated prevalence rates at 40% for PAU in the UK (Popova et al., 2017), and the literature

proposes that for this rate, an appropriate sample size is 92 and 576 for moderate and very low margin errors, respectively (Hajian-Tilaki, 2011).

Data analysis

Statistical analyses were conducted using IBM SPSS Statistics (Version 25). Descriptive analysis of the sample was completed with the demographic variables listed above, self-reported prevalence of PAU, and attitudes and knowledge. A series of Wilcoxon signed-rank tests were performed to assess the efficacy of the intervention on attitudes and knowledge towards PAU. Following this a multiple regression analysis was conducted to assess factors predictive of the changes in attitudes and knowledge following the intervention. Predictive variables were age, level of education, marital status, year of pregnancy, knowledge of CMO guidance on PAU and pre-attitude and knowledge scores. These were re-categorised (as depicted in Table 1) and dummy variables created for age, level of education and year of pregnancy as these were categorical in nature. Marital status was dichotomised into partner/no partner, and pre-attitude score was measured as a continuous variable.

Data screening

Data was screened to test that it met statistical assumptions. Due to the ordinal nature of the data, Wilcoxon-signed rank tests were conducted to determine the efficacy of the intervention. Cases with missing data were omitted and analyses conducted for full data sets only. Difference scores were approximately symmetrically distributed, as indicated by a histogram and Shapiro Wilk statistic of $p = .94$.

Tests of skewness and kurtosis indicated that the data was not normally distributed for both pre- and post-intervention scores on the attitude and knowledge measure ($z = 11.95$ and $z = 14.69$ respectively). This was also observed by Shapiro Wilk's test for normal distribution ($p < .05$). However, research indicates that larger sample sizes are likely to be overly sensitive to statistical tests of deviation, and minor deviations can produce significant p values (Uttley, 2019). Given the W statistic was large for both pre- and post-attitude data ($p = .94$ and $p = .92$ respectively), the deviation was considered to be minor and Wilcoxon Signed Rank tests were therefore completed.

Assumptions for parametric tests were met for multiple regression; independence of residuals was indicated by a Durbin-Watson statistic of .707, there was no evidence of multicollinearity as observed by tolerance values great than 0.1, values for Cook's distance above 1, and visual inspection of a Q-Q plot indicated normality. Histograms and boxplots highlighted a violation of assumption of outliers. There were 13 outliers, as indicated by standardised residual values greater than 3, and so were removed prior to statistical analysis.

Results

Demographics

Overall, 1663 participants followed the link for the study and 1536 (92%) consented to take part. The typical respondent was 33.3 years of age (*SD*= 4.89), white (98%), married or cohabiting with a partner (92.4%) and had completed a bachelor's degree or higher (73%). Demographic characteristics are illustrated below in Table 1.

Table 1

Demographic Characteristics of Participants

Characteristic	***N***	**%**
Age *(n* = 1456)		
19-25	90	6.2
26-35	895	61.5
36-50	471	32.3
Ethnicity (*n* = 1468)		
White (UK)	1282	87.3
White (Other)	160	10.9
Other	26	1.8
Marital Status (*n* = 1412)		
Married	970	68.7
Co-habiting	335	23.7
Other	107	7.6
Employment Status (*n* = 1454)		
Employed Full-time/Part-time	942	64.8
Maternity leave	323	22.2
Student/Unemployed/Unable to work	189	13.0
Highest qualification received (*n* = 1463)		
Standard grades/GCSE level or Highers	238	16.3
Bachelor's Degree or higher	1070	73.1
Other	155	10.6
Mental Health Status (*n* = 1468)		
Excellent	137	9.3
Very good	407	27.7
Good	456	31.1
Fair	378	25.8
Poor	90	6.1
Location during pregnancy (*n* = 1463)		
Scotland	692	47.3
England	555	37.9
Wales	115	7.9
Northern Ireland	101	6.9
Year of pregnancy (*n* = 1467)		
Currently pregnant/2020	447	30.5
2016-2019	1020	69.5
Pregnancy (*n* = 1467)		

Planned	1214	82.8
Unplanned	253	17.2
When found out about pregnancy (*n* = 1468)		
Within first 6 weeks	1351	92.0
1st trimester	99	6.7
2nd trimester	15	1.0
3rd trimester	3	0.2

Prevalence

The majority of the sample had consumed alcohol before (98%, *n* = 1331). Information on alcohol consumption prior to finding out they were pregnant and during their pregnancy was gathered using the AUDIT-C (illustrated in Table 2). UK standard units and scoring system were utilised, and participant's scores were calculated as per recommended for use in clinical practice. Scores range from 0-12, with below 5 indicating "lower risk drinking" and 5+ indicating the need for further screening to assess "risky" drinking.

Table 2

Alcohol Consumption on the AUDIT-C Questionnaire at Two Time Points: Before Participants Found Out they were Pregnant and During the Pregnancy

Audit-C	**Before** ***n*** **(%)**	**During** ***n*** **(%)**
Frequency of drinking	*(n = 1358)*	*(n = 1356)*
Never	52 (3.8%)	1014 (74.8%)
Monthly or less	379 (27.9%)	289 (21.3%)
2-4 times per month	497 (36.6%)	46 (3.4%)
2-3 times per week	347 (25.6%)	7 (0.5%)
4+ times per week	83 (6.1%)	0 (0%)
Quantity consumed on typical day of drinking in standard UK units	*(n = 1358)*	*(n = 1357)*
0	161 (11.9%)	1061 (78.2%)
1-2	431 (31.7%)	288 (21.2%)
3-4	382 (28.1%)	5 (0.4%)
5-6	215 (15.8%)	2 (0.1%)
7-9	103 (7.6%)	1 (0.1%)
10 or more	66 (4.9%)	0 (0%)
Frequency of heavy episodic drinking (6 or more units per occasion)	*(n = 1357)*	*(n = 1357)*

Never	240 (17.7%)	1343 (99.0%)
Less than monthly	681 (50.2%)	11 (0.8%)
Monthly	277 (20.4%)	1 (0.1%)
Weekly	155 (11.4%)	2 (0.1%)
Daily or almost daily	4 (0.3%)	0 (0%)
Audit Score	*(n = 1357)*	*(n = 1354)*
<5 (“lower risk drinking”)	833 (61.4%)	1351 (99.8%)
5+ (further screening required)	524 (38.6%)	3 (0.2%)

Note. “Before” refers to alcohol consumption before women found out about the pregnancy, and could represent consumption prior to or following conception.

A reduction in the frequency and quantity of alcohol consumed and frequency of binge drinking was observed from “before they found out they were pregnant” to “during their pregnancy”. AUDIT-C scores also reduced; the mean score before finding out about the pregnancy was 4.11 (*SD*=2.19, *Mdn* = 4.0), and during pregnancy was 0.32 (*SD*= 0.64, *Mdn* = 0.0).

Women were also asked about changes to their alcohol consumption when they found they were pregnant. The majority of participants stopped drinking alcohol completely (*n* = 981, 78.7%) and a further 204 (16.4%) continued to drink on special occasions only. Only three participants (0.2%) reported they continued “to drink the same amount as before”, no participants increased intake and 4.7% reduced their intake.

Impact of intervention

Attitude and Knowledge

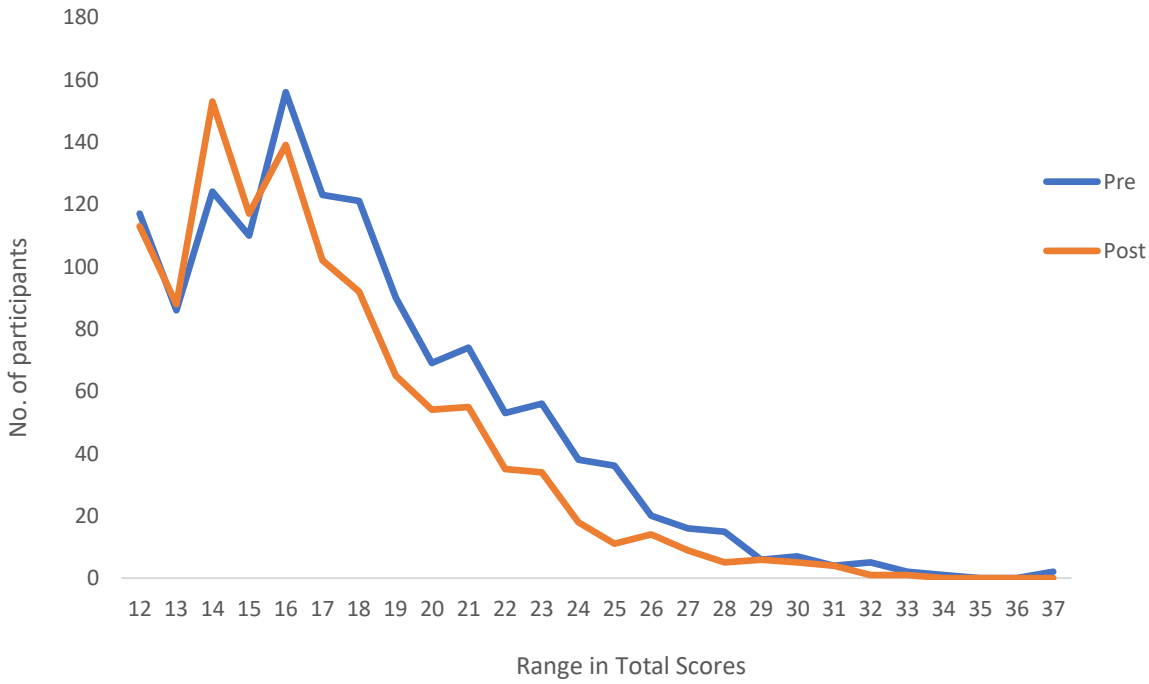
1331 participants provided responses to the ‘Attitude & Knowledge Towards Drinking During Pregnancy Scale’ prior to the intervention and 1120 post-intervention, an attrition rate of 16% (*n* = 211).

To assess differences between pre and post scores following the intervention responses to all 12 statements were collated and scored to provide total scores and means. Statements 3 and 4 were re-coded in order for the dataset to point in the same direction across items and scores ranged from 12 (negative attitude) to 60 (positive attitude). Of the 1120 participants, 47% (*n* = 527) responded more negatively towards PAU following the intervention, whilst

there were no differences in attitudes for 29% (n = 326). A Wilcoxon signed rank-test determined there was a statistically significant median decrease in positive attitudes towards drinking following the intervention (*Mdn* = 16) compared to attitudes prior to the intervention (*Mdn* = 17) with a small effect size, z = -9.67, p < .001 r = 0.29. This is illustrated below in Figure 1.

Figure 1

Participants Total Scores on Attitude and Knowledge Measure Pre- and Post-intervention



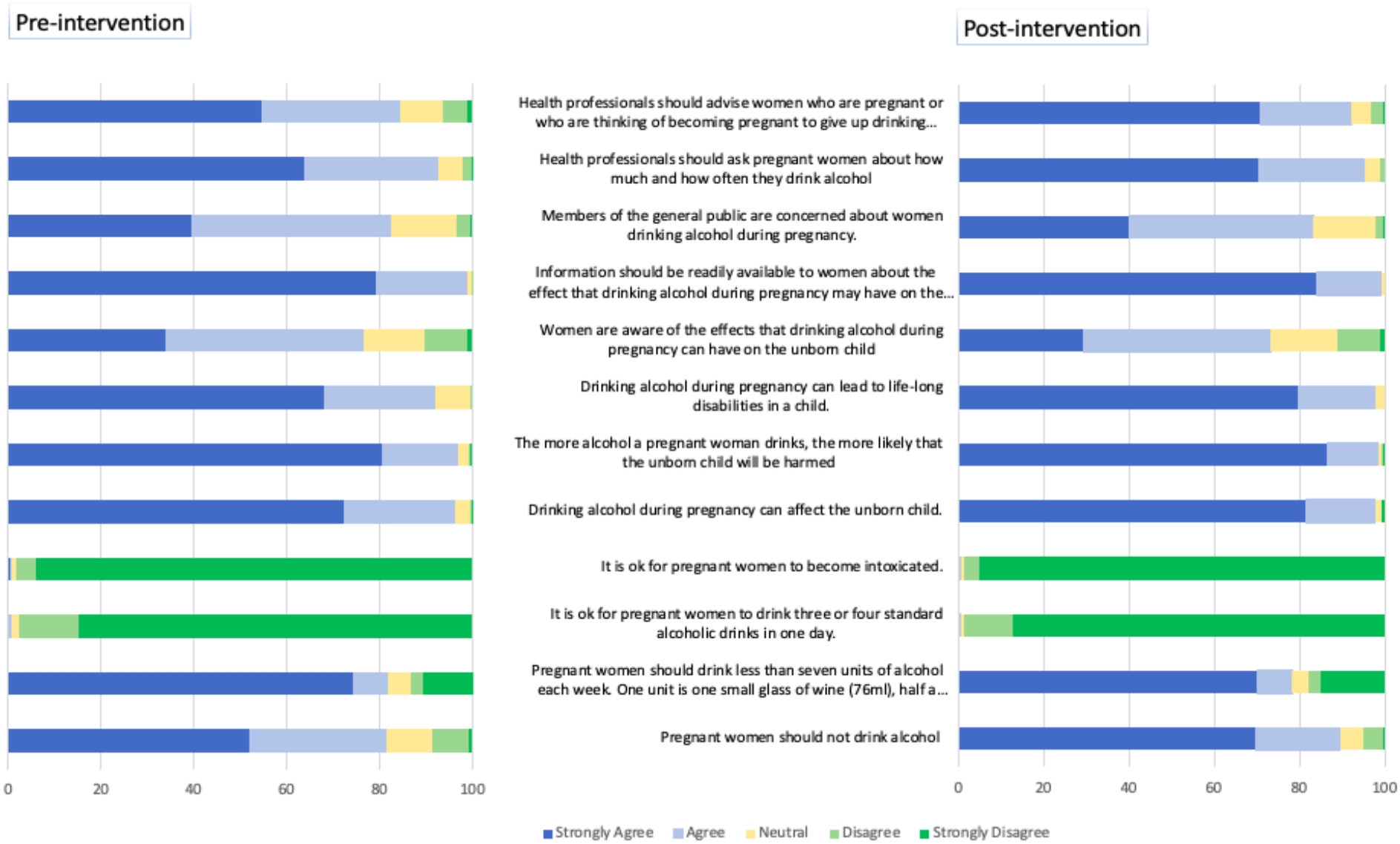
Note. Scores range from 12-60, with lower scores indicating more negative attitudes towards PAU.

The majority of participants demonstrated negative attitudes towards PAU, which increased following the intervention. For example, four out of 5 participants agreed that pregnant women should not drink alcohol (81.5%) pre-intervention, which increased to 89.6% post-intervention. 8.6% of women disagreed with this statement prior to the intervention, compared to 5% post-intervention. Secondly, more participants reported stronger agreement/disagreement with statements following the intervention. For example, more women strongly agreed that drinking could lead to lifelong disabilities in a child following the

intervention than before (79.3% and 68.0% respectively). Pre and post scores are illustrated below in Figure 2.

Figure 2

Pre- and Post-intervention Individual Scores on the 'Attitude and knowledge Towards Drinking in Pregnancy' Scale

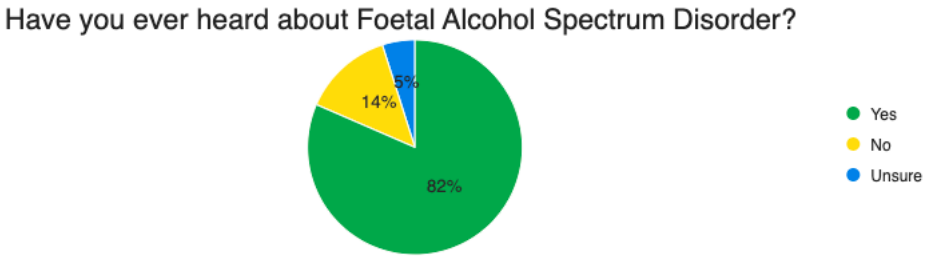


Knowledge of risks of PAU and guidance

The majority of participants had heard of the term Foetal Alcohol Spectrum Disorder (see Figure 3), and were aware of the CMO's guidance (85.5%, *n* = 1130). When asked to respond to the following item: "There is no safe amount of alcohol during pregnancy. Do you feel that this message is widely known throughout the UK?", 37.2% of participants reported "no" (*n* = 491), 21.7% (*n* = 287) were unsure, and 41.1% of participants reported "yes" (*n* = 543).

Figure 3

Knowledge of Term FASD



Several Wilcoxon signed-rank tests were conducted to determine differences in knowledge post-intervention. Difference scores were approximately symmetrically distributed, as assessed by visual inspection of histograms on each item. Table 3 below illustrates scores pre- and post-intervention.

Table 3

Knowledge of Effects of PAU and Level of Agreement with UK CMO's Guidance

		Pre-intervention		Post-Intervention			
Knowledge	***N***	***M (SD)***	***Mdn***	***M (SD)***	***Mdn***	***Z***	***r***
PAE increases risks of:							
1. Miscarriage	1103	1.91 (0.89)	2.0	1.39 (0.68)	1.0	-18.05***	0.54
2. Infantile withdrawal symptoms	1096	1.64 (0.77)	1.0	1.43 (0.73)	1.0	-8.8***	0.27
3. Low birth weight	1091	1.58 (0.67)	1.0	1.33 (0.58)	1.0	-12.1***	0.37
4. Seizures	1097	2.12 (0.85)	2.0	1.77 (0.88)	2.0	-11.7***	0.35
5. Birth defects/malformations	1095	1.77(0.79)	2.0	1.38 (0.64)	1.0	-15.5***	0.47
6. Lower IQ	1098	2.08 (0.92)	2.0	1.60 (0.82)	1.0	-17.3***	0.52
Agreement with guidance there is no safe level	1091	1.68 (1.03)	1.0	1.44 (0.84)	1.0	-10.3***	0.31
Agreement with guidance to abstain	1113	1.69 (1.05)	1.0	1.50 (0.92)	1.0	-9.5***	0.28

*** $p < .001$

Note. Response options were 1 (*strongly agree*), 2 (*agree*), 3 (*neither agree nor disagree*), 4 (*disagree*), 5 (*strongly disagree*). Scores above are representative of these; for example, a median score of 2 equates to "agree".

Significant differences were observed between pre and post intervention on all items assessing knowledge of risks associated with PAU and level of agreement with the UK CMO's guidance. Effect sizes ranged from moderate to large as indicated by *r* (Cohen, 1988; Fritz et al., 2012).

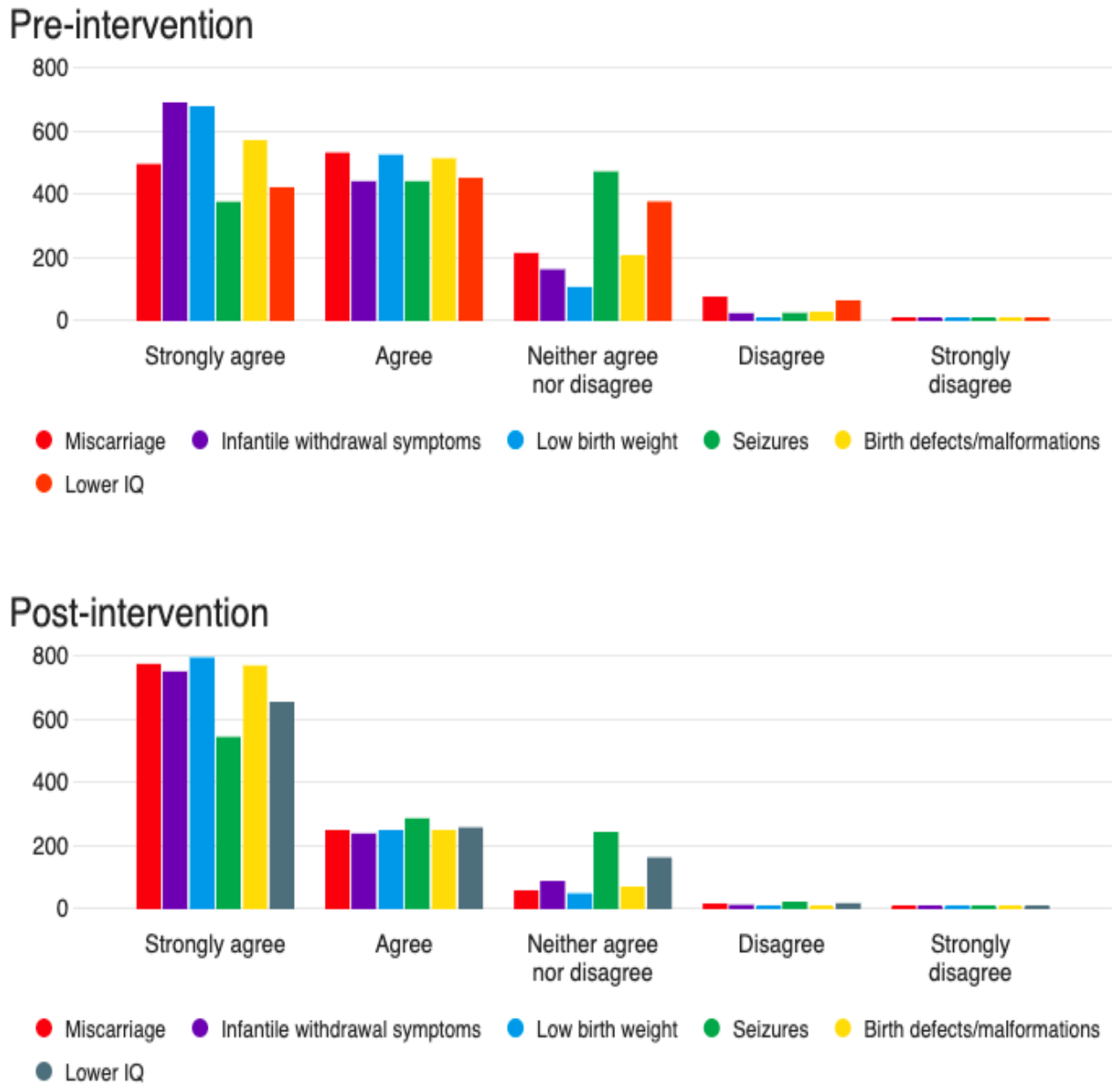
An increase of 7.5% was observed for agreement with the guidance that there is no safe level of alcohol use during pregnancy following the intervention, and 5.8% fewer disagreed with this post-intervention. Additionally, there was a 9.1% increase in those who strongly

agreed with the guidance that women should avoid alcohol during pregnancy post-intervention, and a 3.9% decrease in those who disagreed with this statement (from 11.2% to 7.3%).

Participants agreed more strongly with statements of risks associated with PAU following the intervention. For example, there was a statistically significant increase of 32.9% in those who strongly agreed that PAU increases the chance of miscarriage, and a decrease in those who disagreed from 6.1% to 1.8% following the intervention. Large effect sizes were observed particularly for this and lower IQ. This shift in knowledge was observed across the items (see Figure 4 below).

Figure 4

Knowledge of Risks Pre and Post-intervention



Factors predictive of change

A multiple regression was conducted to explore whether demographic variables predicted the differences observed in attitudes and knowledge following the intervention. The model predicted statistically significant change scores in attitude and knowledge with a medium effect, F (12, 1047) = 25.838, p < .001, adj. R^2 = .22. Regression coefficients and standard errors are illustrated in Table 4 below.

Table 4

Multiple Regression Results for Change Scores in Attitudes and Knowledge

Change Score	*B*	95% CI for B		*SE B*	β	R^2	*Adj.* R^2
		LL	*UL*				
Model						.23	.22**
Constant	4.127	3.143	5.111	.502			
Age (36-50) [Reference category]							
Age (19-25)	.472	-.238	1.183	.362	.039		
Age (26-35)	-.066	-.389	.257	.165	-.012		
Postgraduate Education [Reference category]							
Education (Standard/Highers)	-.211	-.662	.239	.230	-.029		
Education (Bachelor's Degree)	-.525	-.861	-.188	.172	-.094*		
Education (Other/trade)	-.864	-1.376	-.352	.261	-.097*		
Year of pregnancy (2019) [Reference category]							
Year of pregnancy (2020)	.230	-.142	.602	.190	.039		
Year of pregnancy (2018)	.248	-.172	.668	.214	.037		
Year of pregnancy (2017)	.361	-.152	.874	.261	.042		
Year of pregnancy (2016)	-.044	-.591	.502	.278	-.005		
Marital status	.371	-.231	.972	.307	.034		
Knowledge of CMO guidance	.012	-.406	.430	.213	.002		
Pre-attitude and knowledge score	-.293	-.327	-.259	.017	-.465**		

Note. Model = "Enter" method in SPSS Statistics Version 25. *B* = unstandardised regression coefficient; CI = confidence interval *LL* = lower limit; *UL* = upper limit; *SE B* = standard error of the coefficient; β = standardised coefficient; R^2 = coefficient of determination; Adj. R^2 = adjusted R^2.

As 'age', 'education' and 'year of pregnancy' were categorical variables, these were dummy coded. 'Age (36-50)', 'postgraduate education' and 'year of pregnancy (2019)' were reference groups.

*$p < .01$. **$p < .001$

Results illustrated that education (Bachelor's degree or other/trade qualification) and initial score on the measure explained significant proportions of variance in the change score. Those who scored higher on the measure i.e., who already had more negative attitude towards PAU were predicted to have a lower change score.

Following analysis of the output and closer inspection of results, multicollinearity was suspected within the dummy variables. A further comparison of the same dataset was therefore conducted utilising a stepwise regression model to assess which factors contributed the most to predicting change in attitudes and knowledge. Results are indicated below in table 5.

Table 5

Stepwise Regression Results for Change Scores in Attitudes and Knowledge

Change Score	***B***	***SE B***	**β**	***R²***	***Adj. R²***
Model 1				.23	.23***
Constant	5.105	.377			
Pre-attitude and knowledge score	-.332	.021	-.476***		
Model 2				.23	.23*
Constant	5.036	.377			
Pre-attitude and knowledge score	-.338	.021	-.484***		
Post-graduate education	.432	.180	.071*		
Model 3				.23	.23*
Constant	4.273	.539			
Pre-attitude and knowledge score	-.339	.021	-.487***		
Post-graduate education	.470	.181	.078*		
Marital status	.730	.369	.059*		

Note. Model = "Stepwise" method in SPSS Statistics Version 25. *B* = unstandardised regression coefficient; CI = confidence interval *LL* = lower limit; *UL* = upper limit; *SE B* = standard error of the coefficient; β = standardised coefficient; R^2 = coefficient of determination; Adj. R^2 = adjusted R^2.

*$p < .05$, **$p < .01$. ***$p < .001$

The most significant predictor to emerge was the pre-intervention score on the attitude and knowledge scale accounting for 23% of the variance of the model [F (1, 880) = 258.33, $p < .001$, adj. $R^2 = .23$]. Having a post-graduate education and marital status also contributed significantly to the model [F (2, 879) = 132.73, $p < .05$, adj. $R^2 = .23$.] and [F (3, 878) = 90.08, $p < .05$, adj. $R^2 = .23$.], respectively.

Discussion

Main findings

This study provides contemporary national data from a self-selected sample of women in the UK on the prevalence of alcohol consumption in pregnancy, and their attitudes and knowledge of the risks associated with PAU. It also explores the impact of an educational intervention on attitudes and knowledge.

Data on the prevalence of alcohol consumption highlights several points of interest. General alcohol consumption in the sample was high and the majority of women (82%) reported heavy episodic drinking prior to recognition of pregnancy. This is higher than rates of pre-pregnancy binge drinking observed by other studies. A cross-cohort comparison of multi-centre population-based studies conducted by O'Keeffe et al. (2015) illustrated prevalence rates of 59% in the Irish 'SCOPE' study and 24% in the multicentre 'PRAMS' study, although the criteria used in these studies is not clear. Additionally, a significant proportion of women in this study (39%) scored above the threshold (≥ 5) on the AUDIT-C for 'high risk of harm', indicating their consumption was at a harmful level for their health, and their baby's health, if in the early stages of pregnancy. Further screening and targeted prevention such as a referral to specialist alcohol services would have been prompted as a result of these scores, regardless of whether they were pregnant.

A marked decline in consumption following recognition was observed and is consistent with the patterns noted in the literature; namely that a peak in binge drinking is observed around the period of conception which then reduces to a low level at the time of recognition (Kesmodel, 2001). Three out of four women reported 'never' drinking alcohol during pregnancy, and 99% reporting no binge drinking. This abstinence or significant reduction in PAU following recognition mirrors previous studies across countries including Scotland (Wolfson, 2018), Australia (Cameron et al., 2013; McCormack et al., 2017), and Canada (Tough et al., 2006). Despite this trend in consumption, research has indicated prevalence rates of PAU to be approximately 40% using self-reported measures (O'Keeffe et al., 2015) and biological markers and (Popova et al., 2017). In this study 25% of women continued to drink during pregnancy following recognition. Additionally, 21% reported drinking monthly or less, and reported consuming a quantity of 1-2 units on a 'typical day of drinking'. Although these rates are lower, they emphasize that PAU remains a concern in women in the UK even in a

sample that is predominantly comprised of women who were married, had high levels of education and had planned their pregnancy.

Findings on attitudes and knowledge towards PAU were encouraging. The majority of women in this study held negative attitudes towards PAU and were in agreement with the UK's CMO's guidance that pregnant women should not drink alcohol even before exposure to a leaflet on the subject. This is in accordance with qualitative research, which has demonstrated support for this abstinence message, although has iterated that endorsement of such a message does not necessarily equate to its adherence (Holland et al., 2016). Moreover, nearly all women disagreed that it was okay for pregnant women to become intoxicated and concurred that PAU carried risks to the foetus, as also observed by Esposito et al. (2015). Additionally, most women agreed that health professionals should ask pregnant women about their alcohol consumption. Although most women agreed that PAU carried risks, this did not necessarily translate to specific knowledge about FASD or the UK CMO's guidance. In this study, 82% of women had heard of FASD, slightly less than that observed in a Canadian survey where 88% had heard of FAS/FASD (Environics Research Group, 2006). A further 15% had not heard of the UK CMO's guidance on PAU, and two out of five women reported that they felt the message of abstinence was not widely known throughout the UK. This indicates a need for further public health campaigns to raise awareness of the risks throughout our society.

The intervention employed had a positive impact on attitudes and knowledge. Although attitudes of women in this study towards PAU were predominantly negative, significant positive changes were observed as a result of the information leaflet. Women were significantly more knowledgeable about the specific risks associated with PAU and a larger proportion of women were in agreement with the UK's guidance on abstinence following the intervention. Additionally, attitudes shifted from more neutral standpoints to stronger disagreement with PAU. Pre-existing attitudes, knowledge and education were factors predictive of these changes, as those with less negative attitudes were more likely to experience change following the intervention. Results were subtle but promising and provide support for the utility of education interventions in general populations and suggest that those with more impartial views may gain more benefit.

Explanations of this impact on attitudes and knowledge can be drawn from health behaviour literature. As mentioned previously, information regarding health consequences is

an effective BCT for reducing PAU (Fergie et al., 2019). Furthermore, knowledge, personality, attitudes, beliefs, habits, social circumstances and norms are all motivators of health behaviour (Morrison & Bennett, 2009), and as knowledge influences attitude, this results in a change to health behaviour. Although this study did not assess direct behaviour change, it did demonstrate significant changes in attitudes and knowledge of risks and adds to the literature of intervention research in this area.

Strengths and limitations

A key strength of this study is its large sample size and national recruitment of women across the UK. It provides novel information on self-reported prevalence of PAU in the UK and on the role of an educational intervention on attitudes and knowledge towards PAU. Furthermore, its anonymous nature and use of validated questionnaires to assess prevalence is likely to have facilitated more transparent and accurate reporting of PAU, thus hoping to mitigate risks of reporting and measurement bias.

This study is not without its shortcomings, however. Firstly, the representativeness of the sample is a limitation that must be considered. The majority of respondents were white married women, with high levels of education and predominantly negative attitudes towards PAU. Populations of younger women, women of different ethnic origins, those in lower SES groups and with lower levels of education were underrepresented in this study. The average age of the sample was 33.3 years, which is higher than the average age of mothers in England and Wales (30.7 years) as recorded in 2019 (Office for National Statistics, 2019), and in Scotland (31 years in 2018) (The Scottish Public Health Observatory, 2020). Alongside homogeneity of the sample, 83% of women in this study reported their pregnancies as planned and had found out about their pregnancy in the first 6 weeks. This is disproportionate to national data, which indicates that in the UK over 40% of pregnancies are unplanned (Rudd et al, 2013), and consequently, these findings may lack generalisability to other populations, even within the UK.

Secondly, the methodology of the study has its limitations. The most common method of measuring PAU is via maternal self-reports; however, research has consistently demonstrated these are likely to underestimate prevalence rates (Howlett et al., 2018; Lange et al., 2014; McQuire et al., 2019). PAU is an emotive and sensitive topic, and unsurprisingly

social desirability bias, recall bias and use of complex and subjective language are all existing barriers to accurate self-reporting in cross sectional studies (Muggli et al., 2015). This study attempted to mitigate these risks via anonymous recruitment, however these factors must be considered. It is also possible that drinking behaviour influenced participants' decision to take part in the study as women with heavier PAU may be less likely to participate, resulting in disproportionate prevalence estimates and less diverse attitudes and knowledge. In addition to this, despite recruiting a large sample size, the risk of this study being overpowered must be considered. The probability of Type 1 errors increase with larger sample sizes as there is more potential for effects with small statistical significance to be detected (Lenth, 2001). Results of the intervention, more specifically effect sizes observed between pre, and post intervention scores should therefore be interpreted with caution.

Furthermore, due to the phrasing of questions, conclusions regarding PAU prior to recognition of pregnancy are limited. This study asked women about consumption during pregnancy and before they found out they were pregnant. This phrasing, "before you found out you were pregnant" could have been improved to ensure women were retrospectively reporting on consumption during the period in which they had conceived but were not yet aware of the pregnancy. Thus, any conclusions drawn based upon risks of associated PAU at the first time point are limited and could represent consumption either before or after conception. As the data can only conclude about PAU following recognition, this may have driven down prevalence rates. Results may have also led to different conclusions dependent on the method of analysis employed. Subgroup analysis by the year of pregnancy in which women reported and, whether women consumed alcohol during pregnancy or not, could have led to different results on the efficacy of the intervention. Sensitivity analyses could therefore have been performed on such subgroup analyses in order to assess if findings would have remained consistent with those found and if so, strengthen the conclusions drawn on intervention effects.

Clinical implications and future research

Educational interventions such as the one used in this study appears to hold promise in changing attitudes and improving knowledge of the risks of PAU and thus should be regarded as appropriate interventions for general populations. Ease of delivery, cost-efficacy and equitability are some of the major advantages of such interventions, which can be delivered in multiple formats (online/paper/face to face/postal) and across a variety of settings. Whilst

online delivery of interventions offers considerable advantages, the question as to whether online surveys can reach representative samples must be considered. More extensive research investigating the efficacy of such interventions across a range of cohorts including younger women of childbearing age, substance misuse populations and ethnic minorities is recommended. In addition, given the patterns observed across studies of high level of consumption in pre-conception stages, efforts of healthcare professionals should be targeted towards women of childbearing years and not just pregnant women, to reduce risk of inadvertent exposure at an earlier stage and subsequently, the prevalence of FASD.

Interestingly, the results of this study may offer some insight into the mechanisms by which educational or public health interventions for PAU and FASD operate. More specifically, results of the exploratory regression indicate that attitude and knowledge were the most significant predictors of change following the intervention, thus pointing towards a need for an educational and preventative focus of interventions aimed at reducing risk of FASD. Consideration of timing of implementation may also be important, as earlier education of risks of PAU as in secondary schools may be more protective against future use of alcohol. Universal preventative school-based interventions on alcohol use amongst adolescents has been shown to have small but positive effects, with possible longer term health gains (Strøm et al., 2014). Social determinants of health are therefore likely to be important factors impacting the efficacy of preventative educational interventions, and further research exploring these is warranted.

Conclusion

This study is the first of its kind to assess PAU in a self-selected sample of women in the UK, and the impact of an education intervention on attitudes and knowledge of risks. Findings identified that although the level of consumption was low, 25% of women continued to drink during pregnancy. The information leaflet had a positive impact and findings provide support for the utility of brief educational interventions in increasing knowledge of harm caused by prenatal alcohol consumption and reducing positive attitudes towards PAU. Implementation of such interventions at community and clinical levels could reduce PAU in the UK and thereby reduce the prevalence of FASD and other adverse pregnancy outcomes.

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Appendices

Appendix A: Submission guidelines for Journal BMC Pregnancy and Childbirth

Aims & Scope:

BMC Pregnancy & Childbirth is an open access, peer-reviewed journal that considers articles on all aspects of pregnancy and childbirth. The journal welcomes submissions on the biomedical aspects of pregnancy, breastfeeding, labor, maternal health, maternity care, trends and sociological aspects of pregnancy and childbirth.

Author guidelines:

Research article criteria

Research articles should report on original primary research, but may report on systematic reviews of published research provided they adhere to the appropriate reporting guidelines which are detailed in our editorial policies. Please note that non-commissioned pooled analyses of selected published research will not be considered. Studies reporting descriptive results from a single institution will only be considered if analogous data have not been previously published in a peer reviewed journal and the conclusions provide distinct insights that are of relevance to a regional or international audience.

BMC Pregnancy and Childbirth strongly encourages that all datasets on which the conclusions of the paper rely should be available to readers. We encourage authors to ensure that their datasets are either deposited in publicly available repositories (where available and appropriate) or presented in the main manuscript or additional supporting files whenever possible. Please see Springer Nature's information on recommended repositories. Where a widely established research community expectation for data archiving in public repositories exists, submission to a community-endorsed, public repository is mandatory. A list of data where deposition is required, with the appropriate repositories, can be found on the Editorial Policies Page.

Preparing your manuscript

The information below details the section headings that you should include in your manuscript and what information should be within each section.

Please note that your manuscript must include a 'Declarations' section including all of the subheadings (please see below for more information).

Title page

The title page should:

present a title that includes, if appropriate, the study design e.g.:

"A versus B in the treatment of C: a randomized controlled trial", "X is a risk factor for Y: a case control study", "What is the impact of factor X on subject Y: A systematic review"

or for non-clinical or non-research studies a description of what the article reports

list the full names and institutional addresses for all authors

if a collaboration group should be listed as an author, please list the Group name as an author. If you would like the names of the individual members of the Group to be searchable through their individual PubMed records, please include this information in the "Acknowledgements" section in accordance with the instructions below

indicate the corresponding author

Abstract

The Abstract should not exceed 350 words. Please minimize the use of abbreviations and do not cite references in the abstract. Reports of randomized controlled trials should follow the CONSORT extension for abstracts. The abstract must include the following separate sections:

Background: the context and purpose of the study

Methods: how the study was performed and statistical tests used

Results: the main findings

Conclusions: brief summary and potential implications

Trial registration: If your article reports the results of a health care intervention on human participants, it must be registered in an appropriate registry and the registration number and date of registration should be in stated in this section. If it was not registered prospectively (before enrollment of the first participant), you should include the words 'retrospectively registered'. See our editorial policies for more information on trial registration

Keywords
Three to ten keywords representing the main content of the article.
Background
The Background section should explain the background to the study, its aims, a summary of the existing literature and why this study was necessary or its contribution to the field.
Methods
The methods section should include: the aim, design and setting of the study the characteristics of participants or description of materials a clear description of all processes, interventions and comparisons. Generic drug names should generally be used. When proprietary brands are used in research, include the brand names in parentheses, the type of statistical analysis used, including a power calculation if appropriate
Results
This should include the findings of the study including, if appropriate, results of statistical analysis which must be included either in the text or as tables and figures.
Discussion
This section should discuss the implications of the findings in context of existing research and highlight limitations of the study.
Conclusions
This should state clearly the main conclusions and provide an explanation of the importance and relevance of the study reported.
List of abbreviations
If abbreviations are used in the text they should be defined in the text at first use, and a list of abbreviations should be provided.
Declarations
All manuscripts must contain the following sections under the heading 'Declarations':
Ethics approval and consent to participate
Consent for publication
Availability of data and materials
Competing interests
Funding
Authors' contributions
Acknowledgements
Authors' information (optional)
Please see below for details on the information to be included in these sections.
If any of the sections are not relevant to your manuscript, please include the heading and write 'Not applicable' for that section.
Ethics approval and consent to participate
Manuscripts reporting studies involving human participants, human data or human tissue must:
include a statement on ethics approval and consent (even where the need for approval was waived)
include the name of the ethics committee that approved the study and the committee's reference number if appropriate
Studies involving animals must include a statement on ethics approval and for experimental studies involving client-owned animals, authors must also include a statement on informed consent from the client or owner.
See our editorial policies for more information.
If your manuscript does not report on or involve the use of any animal or human data or tissue, please state "Not applicable" in this section.
Consent for publication
If your manuscript contains any individual person's data in any form (including any individual details, images or videos), consent for publication must be obtained from that person, or in the case of children, their parent or legal guardian. All presentations of case reports must have consent for publication.
You can use your institutional consent form or our consent form if you prefer. You should not send the form to us on submission, but we may request to see a copy at any stage (including after publication).
See our editorial policies for more information on consent for publication.
If your manuscript does not contain data from any individual person, please state "Not applicable" in this section.
Availability of data and materials

All manuscripts must include an ‘Availability of data and materials’ statement. Data availability statements should include information on where data supporting the results reported in the article can be found including, where applicable, hyperlinks to publicly archived datasets analysed or generated during the study. By data we mean the minimal dataset that would be necessary to interpret, replicate and build upon the findings reported in the article. We recognise it is not always possible to share research data publicly, for instance when individual privacy could be compromised, and in such instances data availability should still be stated in the manuscript along with any conditions for access.
Data availability statements can take one of the following forms (or a combination of more than one if required for multiple datasets):
The datasets generated and/or analysed during the current study are available in the [NAME] repository, [PERSISTENT WEB LINK TO DATASETS]
The datasets used and/or analysed during the current study are available from the corresponding author on reasonable request.
All data generated or analysed during this study are included in this published article [and its supplementary information files].
The datasets generated and/or analysed during the current study are not publicly available due [REASON WHY DATA ARE NOT PUBLIC] but are available from the corresponding author on reasonable request.
Data sharing is not applicable to this article as no datasets were generated or analysed during the current study.
The data that support the findings of this study are available from [third party name] but restrictions apply to the availability of these data, which were used under license for the current study, and so are not publicly available. Data are however available from the authors upon reasonable request and with permission of [third party name].
Not applicable. If your manuscript does not contain any data, please state 'Not applicable' in this section.
More examples of template data availability statements, which include examples of openly available and restricted access datasets, are available here.
BioMed Central also requires that authors cite any publicly available data on which the conclusions of the paper rely in the manuscript. Data citations should include a persistent identifier (such as a DOI) and should ideally be included in the reference list. Citations of datasets, when they appear in the reference list, should include the minimum information recommended by DataCite and follow journal style. Dataset identifiers including DOIs should be expressed as full URLs. For example: Hao Z, AghaKouchak A, Nakhjiri N, Farahmand A. Global integrated drought monitoring and prediction system (GIDMaPS) data sets. figshare. 2014. http://dx.doi.org/10.6084/m9.figshare.853801
With the corresponding text in the Availability of data and materials statement:
The datasets generated during and/or analysed during the current study are available in the [NAME] repository, [PERSISTENT WEB LINK TO DATASETS].[Reference number]
If you wish to co-submit a data note describing your data to be published in *BMC Research Notes*, you can do so by visiting our submission portal. Data notes support open data and help authors to comply with funder policies on data sharing. Co-published data notes will be linked to the research article the data support (example).
Competing interests
All financial and non-financial competing interests must be declared in this section.
See our editorial policies for a full explanation of competing interests. If you are unsure whether you or any of your co-authors have a competing interest please contact the editorial office.
Please use the authors initials to refer to each authors' competing interests in this section.
If you do not have any competing interests, please state "The authors declare that they have no competing interests" in this section.
Funding
All sources of funding for the research reported should be declared. The role of the funding body in the design of the study and collection, analysis, and interpretation of data and in writing the manuscript should be declared.
Authors' contributions
The individual contributions of authors to the manuscript should be specified in this section. Guidance and criteria for authorship can be found in our editorial policies.
Please use initials to refer to each author's contribution in this section, for example: "FC analyzed and interpreted the patient data regarding the hematological disease and the transplant. RH performed the

histological examination of the kidney, and was a major contributor in writing the manuscript. All authors read and approved the final manuscript."

Acknowledgements

Please acknowledge anyone who contributed towards the article who does not meet the criteria for authorship including anyone who provided professional writing services or materials.

Authors should obtain permission to acknowledge from all those mentioned in the Acknowledgements section.

See our editorial policies for a full explanation of acknowledgements and authorship criteria.

If you do not have anyone to acknowledge, please write "Not applicable" in this section.

Group authorship (for manuscripts involving a collaboration group): if you would like the names of the individual members of a collaboration Group to be searchable through their individual PubMed records, please ensure that the title of the collaboration Group is included on the title page and in the submission system and also include collaborating author names as the last paragraph of the “Acknowledgements” section. Please add authors in the format First Name, Middle initial(s) (optional), Last Name. You can add institution or country information for each author if you wish, but this should be consistent across all authors.

Please note that individual names may not be present in the PubMed record at the time a published article is initially included in PubMed as it takes PubMed additional time to code this information.

Authors' information

This section is optional.

You may choose to use this section to include any relevant information about the author(s) that may aid the reader's interpretation of the article, and understand the standpoint of the author(s). This may include details about the authors' qualifications, current positions they hold at institutions or societies, or any other relevant background information. Please refer to authors using their initials. Note this section should not be used to describe any competing interests.

Footnotes

Footnotes can be used to give additional information, which may include the citation of a reference included in the reference list. They should not consist solely of a reference citation, and they should never include the bibliographic details of a reference. They should also not contain any figures or tables.

Footnotes to the text are numbered consecutively; those to tables should be indicated by superscript lower-case letters (or asterisks for significance values and other statistical data). Footnotes to the title or the authors of the article are not given reference symbols.

Always use footnotes instead of endnotes.

References

Examples of the Vancouver reference style are shown below.

See our editorial policies for author guidance on good citation practice

Web links and URLs: All web links and URLs, including links to the authors' own websites, should be given a reference number and included in the reference list rather than within the text of the manuscript. They should be provided in full, including both the title of the site and the URL, as well as the date the site was accessed, in the following format: The Mouse Tumor Biology

Database. http://tumor.informatics.jax.org/mtbwi/index.do. Accessed 20 May 2013. If an author or group of authors can clearly be associated with a web link, such as for weblogs, then they should be included in the reference.

Figures, tables and additional files

See General formatting guidelines for information on how to format figures, tables and additional files.

Appendix B: Ethical approval

Ethics Approval Letter CLIN784

SCHOOL of HEALTH IN SOCIAL SCIENCE

The University of
Edinburgh
Medical School
Doorway 6, Teviot Place

02 March 2021

Dear Orlagh Keating

Application for Ethical Approval

Reference: CLIN784

Project Title: Pregnancy, Alcohol and Behaviour: The impact of an information leaflet on women's attitudes towards drinking during pregnancy

Thank you for submitting the above research project for review by the School of Health in Social Science Research Ethics Committee (REC). I can confirm that the submission has been independently reviewed and was approved on 5th July 2020.

The standard conditions of this approval are:

I. Conduct the project strictly in accordance with the proposal submitted and granted ethics approval, including any amendments made to the proposal required by the REC.

II. Advise the REC (by email to ethics.hiss@ed.ac.uk) of any complaints or other issues in relation to the project which may warrant review of the ethical approval of the project.

III. Make submission for approval of amendments to the approved project before implementing such changes.

IV. Advise in writing if the project has been discontinued.

The School's Research Ethics Policy and further information and resources are available on the School's website.

You may now commence your project; we wish you the best of luck.

Yours sincerely,

Sanni Ahonen

Administrative Secretary
School of Health in Social Science

Appendix C: Research Proposal

Research Proposal

Doctorate in Clinical Psychology

Thesis Research Proposal

(Research 1 Assessment)

This form should be completed and submitted as the assessment for Research 1. It will then be reviewed by a member of the academic team and will receive a grade and detailed feedback. The feedback will include an evaluation of the viability of the project and any recommendations. If there are significant concerns about viability, the project will be flagged to the research director and the research committee will decide whether the project can proceed in its current form.

Word count 5,895

Exam Number
B025436

Provisional Thesis Title
The prevalence of prenatal alcohol consumption in a sample of Scottish women and an exploration of factors associated with this

Proposed Setting
Online questionnaire delivered via Qualtrics survey platform

Allocated Thesis Project Supervisors	
Clinical	
Academic 1	
Academic 2	
Others Involved	

Anticipated Month / Year of Submission
Must be final year for full-time trainees. For flex trainees, the month and year of submission will depend you the individual Training and Development Plan. Trainees from 2011 intake onwards

must submit in May. Trainees who started in 2010 or earlier are advised to submit in May to reduce potential for HCPC registration difficulties.

May 2021

Please Note: Whilst this is not an ethics review process, where questions have some similarities to questions contained in the NHS IRAS Research Ethics form, the corresponding IRAS question numbers are given in parentheses. This is intended to facilitate completion of NHS ethics where such approval is needed.

Section 1: Introduction

1.1 Provide a brief critical review of relevant literature, which should clearly demonstrate the rationale and scientific justification for the research

1000 – 1500 words

Relevant to IRAS A12

Alcohol use in Scotland

Alcohol consumption is a major health, economic and social burden in Scotland, with reports from the Scottish Government indicating costs of £3.6 billion each year in health, social care and crime related services (York Health Economics Consortium, 2010). The Scottish Health Survey conducted in 2017 stated that one in four adults are consuming alcohol at potentially hazardous levels (>14 units per week), and one in six women (McLean et al., 2018). There has been a steady rise in consumption over the past two decades, and this is thought to be associated with lower costs of alcohol, increased choice and easier accessibility, and a shift in cultural attitudes.

Despite alcohol consumption being an integral part of Scottish culture, level of alcohol use is often underreported. This might be related to a general lack of knowledge about the units within drinks and/or social pressures to drink. For example, Sharp et al.'s study in 2014 assessed 1,492 Scottish adults' perceptions of alcohol use. Results highlighted that half of participants were unable to identify the correct number of units in a pint of beer, spirit or a glass of wine, and 41% reported that others would think they were odd if they did not drink at all. Furthermore, the Scottish Health Survey in 2015 identified that adults self-reported 20.8 units of alcohol per week, exceeding the recommended guidelines of 14 units per week. However, these figures only accounted for 55% of total alcohol sales. This renders the question whether Scottish adults are aware of the amount they are consuming, or if they underreport the amount on alcohol screening instruments.

Underreporting of alcohol consumption during pregnancy is a particular public health concern and may be related to the stigma associated with alcohol use during pregnancy. There is relatively little research in this area which could be reflective of the challenges associated with reliable data collection and methodology employed. Some measures appear to be more effective than others in identifying alcohol use, for example self-administered questionnaires have been found to be more sensitive than questionnaires administered by an interviewer in identifying alcohol consumption (Witte & Haile, 1996). Czeizel et al. (2004) investigated the reliability of self-reported information in mothers of children with congenital abnormalities and found low levels of reliability of self-reported information regarding both smoking and alcohol use during pregnancy. This was felt to be due to feelings of guilt and shame, as mothers were concerned of the associations between their alcohol use and smoking and their child's condition. This reporting bias however was not observed in mothers of children without congenital abnormalities who reported more regular alcohol consumption during pregnancy. Public health prevention initiatives often utilise public awareness campaigns such as alcohol warning labels, which can inadvertently increase the stigma and blame associated with alcohol use during pregnancy (Bell et al., 2015).

Prenatal alcohol use

A study recently published in the Lancet indicated that the UK has one of the highest estimated prevalence of alcohol consumption during pregnancy across the globe at 41.3% (Popova et al., 2017). Factors which might be related to this are inconsistencies in medical guidelines and

discrepancies between countries as to safe levels of alcohol during pregnancy. Scottish guidelines had not been revised since 1995 when they were updated on April 1st, 2016 (Alcohol Focus Scotland, 2018). The consensus prior to 2016 was that minimal units were not harmful during pregnancy and guidelines recommended that pregnant women avoid alcohol for the first 3 months, and that "they should drink no more than 1-2 UK units once or twice a week" (NICE, 2008). However current Chief Medical Officer's guideline states that no level of alcohol is safe during pregnancy, and that in order to reduce risks to the unborn baby "the safest approach is not to drink alcohol at all" (Department of Health, 2019). The Scottish Government launched a public awareness campaign around this time known as "No Alcohol No Risk" in an aim to discourage prenatal alcohol use and raise awareness of risks (WHO, 2016).

The use of alcohol during pregnancy, otherwise known as 'prenatal alcohol use' (PAU) is the only direct cause of Foetal Alcohol Syndrome (FAS) or Foetal Alcohol Spectrum Disorder (FASD). FASD is the nondiagnostic umbrella term used to describe the constellation of impairments that result from PAU (Peadon & Elliott, 2010). Research on the impact of alcohol on the developing brain of an unborn baby has only recently been investigated so widely and the global prevalence of FASD is estimated to be 7.7 per 1000 children in the general population (Lange et al., 2017). Studies from Europe and the USA estimated prevalence rates of FASD varying from 1% to 10% of children in the general population (Roozen et al., 2016) (May et al., 2018). More specifically, recent research has proposed that up to 17% of children in the UK are believed to have symptoms consistent with FASD (McQuire et al., 2018).

Children with FASD present with cognitive symptoms including difficulties with executive functioning, attention, memory, communication and sensory/motor impairments. Furthermore, it is associated with challenging behaviour, impairments in academic and social skills, and adolescents with FASD are 19-40 times more likely than the general population to be involved in the criminal justice system (Popova et al., 2011). As alcohol consumption is still prevalent during pregnancy for numerous reasons, it is not surprising that there are a growing number of children in Scotland with FASD and alcohol related neurodevelopmental deficits. The prevalence of FASD and PAU in Scotland is unclear however, and this has been a key area of focus for the Scottish Government over the past 2 years. A recent study in Glasgow investigated the prevalence and patterns of alcohol use during pregnancy through measurement of meconium levels in pregnant women. Researchers confirmed that alcohol consumption during pregnancy is underreported and identified that at least 15% of women were consuming significantly harmful amounts of alcohol during pregnancy (Abernethy et al., 2018).

Challenges

There are numerous challenges with conducting research in this area, one such being the stigma associated with PAU and underreporting of level of consumption. Pregnant women often experience negative judgement from service providers if they disclose alcohol consumption (Poole & Isaac, 2001) causing significant barriers in seeking and obtaining the support they need (Green et al., 2016). Changes in guidelines surrounding PAU and lack of awareness of these, as well as the current culture of alcohol use have further hindered preventative work in the area. Screening methods utilised by healthcare professionals in clinical practice often make mothers feel as though they will be perceived negatively by others or accused of causing harm to their unborn child. This exacerbates the difficulties surrounding diagnoses of FASD, and results in lack of service provision as children are not being identified or supported. Further research is necessary on screening measures which will encourage transparent disclosure about PAU in order to identify children at risk of FASD or neurodevelopmental difficulties as a result of PAU.

Rational for this study

The literature has recommended the need for more effective prevention strategies targeting PAU and for monitoring of children born with FASD (Popova et al., 2017). A guideline proposed by the Scottish Intercollegiate Guidelines Network in 2016 highlighted that research on FASD should be a

high priority, and that because PAU is common across the general population in the UK, the focus should be on altering drinking behaviours at a population level. Recommended strategies include increasing awareness of new guidelines via social marketing campaigns, clearer warning labels on alcoholic drinks, and training healthcare professionals, healthcare workers and criminal justice workers to discuss alcohol consumption with women who are pregnant or seeking advice on conception (Alcohol Focus Scotland, 2017).

Research on alcohol consumption during pregnancy in the general population both globally and in Scotland is limited. Studies have investigated stigma around alcohol consumption during pregnancy, however this has been from the perspective of healthcare professionals rather than the views of biological mothers (Payne et al., 2005). The proposed study aims to address this gap in the literature by investigating the prevalence of alcohol use during pregnancy in Scottish women, and factors associated with this. It aims to explore factors relating to the underreporting of alcohol consumption and assess perceptions of current screening tools used in clinical practice. As this will be conducted via an online anonymised questionnaire, it is hoped that stigma related to alcohol use during pregnancy will be significantly reduced, which will allow the prevalence of PAU to be assessed more transparently. This study aims to highlight the need to target this population at a service level in order to enhance our knowledge about alcohol consumption during pregnancy, identify possible high-risk groups, and make recommendations for healthcare screening and treatment plans.

Section 2: Research Questions / Objectives

2.1 What is the principal research question / objective?
IRAS A10

What is the prevalence of alcohol consumption during pregnancy in a sample of women in Scotland and what are the factors associated with higher levels of consumption?

2.2 What are the secondary research questions / objectives, if applicable?
Keep these focused and concise, with a maximum of 5 research questions
IRAS A11

Is lack of awareness of current guidelines on alcohol consumption associated with higher levels of alcohol use during pregnancy?
Do women feel comfortable answering questions on alcohol consumption using current screening tools?
Are there particular questions used to screen for alcohol consumption during pregnancy which would elicit more accurate responses?
Is lack of disclosure or underreporting of alcohol use during pregnancy associated with perceived levels of stigma and/or feelings of shame/guilt?

Section 3: Methodology

3.1 Give a full summary of your design and methodology
It should be clear exactly what will happen at each stage of the project
IRAS A13

Design
This study will employ a cross-sectional, correlational within-groups design. Participants will be asked to complete an online questionnaire. The dependent variable will be alcohol consumption during pregnancy, as measured using the AUDIT-C questionnaire. The 7 independent variables of interest include demographic factors such as age, socio-economic status, marital status, level of education of alcohol guidelines, employment status, level of engagement with prenatal services, and use of other substances during pregnancy. Each of these will be measured via an online questionnaire.

Ethical approval will be obtained from the Psychology Research Ethics Committee at the University of Edinburgh and from NHS Research Ethics Committee via IRAS.

Participants & recruitment

In order to gain a sufficient sample size, recruitment will take place across multiple platforms online. It aims to recruit women in the Scottish population over the age of 18 who have been pregnant within the previous 10 years. As recommended alcohol guidelines changed in April 2016 this study aims to capture women who have been pregnant before and after this change. Participants must have been in contact with their GP or prenatal services with regard to the pregnancy.

The study intends to recruit a representative sample of the general population as well as those with alcohol difficulties by targeting a range of settings. The study will be advertised via leaflets which will be displayed in multiple locations such as waiting rooms in GP practices, maternity health care services and children's centres. An electronic link to the study will be provided on these leaflets, as well as information on the study. It will also be promoted through social media platforms such as Facebook, Twitter & LinkedIn, and other online organisations relevant to the study such as Mumsnet.

There are certain caveats and ethical considerations of online recruitment to be noted. For example, some online pages such as Facebook groups which are freely accessible to the public may not have a moderator to seek permission from to advertise the study. In this circumstance the trainee will promote transparency and be forthright about their access to the group as a researcher. Permission will be sought to advertise the study from sites where a moderator is available and will comply with the sites' policies and 'terms of use'.

The trainee will inform members within their health board of the study in order to enhance recruitment. Third sector support services such as Alcohol Focus Scotland and alcohol services in the trainee's health board will also be contacted to inform them of research being undertaken and will be posted leaflets to the study which will be placed on noticeboards if permitted.

Procedure

The study will be advertised on leaflets and online platforms and participants will be instructed to follow or enter a link using an Internet browser on their device should they wish to conduct the study. This will direct them to the Qualtrics platform. In order to protect respondent anonymity, the 'Anonymous Link' hyperlink will be employed before distributing the survey which disables the survey from collecting participants IP address.

Firstly, participants will be directed to an information sheet outlining the rationale for the study and what it will involve. Informed consent will be gained by asking the participant to click on a checkbox if they wish to undertake the study before continuing, and subsequently will be directed to the questionnaire. Demographic information will be gathered using a questionnaire which will be designed specifically for the study. Items will be replicated from the Scottish Public Health Observatory surveys on alcohol use and health behaviours in the general public.

Participants will then be required to complete questions regarding their knowledge of current UK drinking guidelines and guidelines specific to pregnancy. They will also be asked about perceived stigma from others when reporting alcohol consumption. Their perceptions of current screening tools such as the CAGE, T-ACE & TWEAK will then be assessed. Following this, the AUDIT-C will be administered to measure self-reported levels of alcohol use during pregnancy. Participants are permitted to withdraw from the study at any point by closing the internet browser they are using. They will be given a choice to save any responses made so additional but incomplete data can also be collected. This will be detailed in the information sheet.

Once participants have completed the questionnaire, they will be directed to a debrief form which will provide relevant contact details should the participant wish to contact other services for information or support following the study. Details of how they can access the findings of the study in the future will be provided, and participants will be given the option of providing their email address should they wish to be contacted with the results of the study once available.

The questionnaire will be designed to maximise the data gathered and minimise participant burden and so it is estimated that the study will take 15 minutes to complete. Prior to any recruitment it will be piloted amongst 5-7 individuals to ensure there are no complications with the questionnaire in terms of its structure or wording of questions.

Data storage
Participants who have completed the study will be assigned a number on the survey platform. There will be no identifiable information as the study is anonymous and all data collected will be gathered on the survey software (Qualtrics). Data will be stored in a single secure data centre on this platform which is GDPR compliant. Access to the database will be permitted only for the trainee and supervisors involved in the study. On completion of the recruitment phase, data will be transferred to an Excel database which will be stored on and NHS network drive, which is backed up daily, as well as the University's SharePoint system. The folder it is contained in will be locked and permitted for use by the trainee and supervisors involved. Once the study has been completed, all data held on Qualtrics and on NHS/University shared drives will be deleted.

3.2.1 In which aspects of the research process have you actively involved, or will you involve, patients, service users and/or their carers or members of the public?
Highlight as appropriate.
IRAS A14-1

Design of the research	Analysis of results
Management of the research	**Dissemination of findings**
Undertaking the research	None of the above

3.2.2 Give details of involvement, or if none, please justify the absence of involvement

Participants will be involved in conducting the research study and providing data to address the research questions. They will also be involved in the dissemination of its findings should they choose to provide their contact details following a debriefing form.

A poster of the study and its results will be presented at NHS departmental conferences and may be placed across relevant venues such as clinic waiting areas in GP surgeries, maternity health care centres, and third sector organisations such as Alcohol Focus Scotland.

3.3 List the principal inclusion and exclusion criteria
IRAS A17-1 and IRAS A17-2

Inclusion:
- Females over the age of 18 who have been pregnant or are currently pregnant, and have had contact with health care professionals regarding their pregnancy
- Have proficient English abilities to enable them to complete the questionnaires

Exclusion:
- Females who have never been pregnant or who have not had contact with NHS services or healthcare professionals in relation to a pregnancy
- Individuals who do not provide informed consent

3.4 How will data be collected?
If quantitative, list proposed measures and justify the use of these measures. If qualitative, explain how data will be collected, giving reasonable detail (don't just say "by interviews".)

Data will be collected via an online questionnaire. Demographic information will be collected at the beginning of the study and will gather the following information:

- Age
- Nationality
- Marital status
- Employment status
- Year of pregnancy
- Socio-economic status
- Level of education
- Previous history of mental health and/or substance use difficulties
- Level of engagement with prenatal services

Participants will then complete a questionnaire assessing their knowledge of recommended guidelines of alcohol use and units in beverages. They will be asked about the information they remember being given during their health checks, for example if they were given advice on dietary supplements such as folic acid, and advise on exercise, alcohol consumption and smoking. They will be asked about whether they may underreport alcohol use for reasons such as perceived stigma from others, lack of knowledge of standard units or guidelines, or due to memory difficulties caused by alcohol use.

Subsequently participants will be asked to rate on a Likert scale how comfortable they would feel answering items on the following screening measures currently used to assess alcohol consumption: CAGE, T-ACE and TWEAK. On each of these scales, scores will range from 0 (least comfortable) to 5 (most comfortable). The CAGE is a 4-item tool (see Appendix 4) used to screen for alcohol dependence difficulties. Participants are required to give a "yes" or "no" response, and a score of 2 or more indicates probable alcohol dependence (Ewing, 1984). Studies have illustrated its reliability and validity in clinical populations (Liskow et al., 1995), however this measure has not been supported for use in the general population. For example Bisson et al. (1999) found the CAGE to have poor criterion validity as it was unable to discriminate between heavy drinkers and non-drinkers in the general population. SIGN guidelines recommend this measure in primary care alongside two qualitative questions on consumption (SIGN, 2003), and has suggested this takes approximately 5 minutes to complete.

The T-ACE is 4 item screening tool based on the CAGE, but has been adapted to assess PAU and to identify individuals engaging in risky drinking behaviours during pregnancy (see appendix 4). Scores on the T-ACE range from 0-5, with a total score of 2 or more indicating greater risks to the developing foetus. Studies have also found this screen to be ineffective in identifying risky or hazardous drinking behaviours in women (Chang et al., 2010). The TWEAK is also a validated measure used to identify risky drinking behaviours in the pregnant population. Both the TWEAK and the T-ACE have been found to have very high specificity rates (99% & 93%, respectively), but poor sensitivity (46-43% and 19-34%, respectively) (Sarkar et al., 2010). SIGN guidelines recommend use of both of these in obstetric settings such as antenatal and preconception consultations (SIGN, 2003).

Following this, participants will be asked to answer questions relevant to their own pregnancy. PAU will be assessed using an adapted version of a measure from recent FASD guidelines (SIGN, 2019) (see Appendix 4). They will also be asked about consumption of other substances which may interfere with prenatal development, including nicotine, prescription and non-prescription drugs, heroin and cocaine. To assess quantity and frequency of alcohol use, the Alcohol Use Disorder Identification Test- Consumption (AUDIT-C) will be utilised (Bush et al., 1998). This self-administered measure is a 3-item alcohol screen recommended for use by SIGN guidelines (see

Appendix 4). Scores range from 0-12, with scores of 1-4 indicating confirmed prenatal alcohol exposure to the foetus, and scores of 5 or greater indicating high risk of exposure. It has been shown to have good validity and efficiency in identifying risky alcohol use and dependency in a diverse range of health and community contexts (de Meneses-Gaya et a., 2009). More specifically, it has been demonstrated as a valid and effective screening tool for hazardous drinking and alcohol dependence in females with appropriate levels of sensitivity and specificity (0.81 and 0.86, respectively) (Bradley et al., 2003). Alcohol unit references will be provided in picture format beside these questions as to inform participants of the units in standard drinks. It is felt that by administering questions in this order, participants may feel more comfortable reporting alcohol use more transparently.

There will a text box provided at the end of the study should participants wish to include any further information or thoughts they have regarding the questions in the study.

Section 4: Sample Size

4.1 What sample size is needed for the research and how did you determine this?
For quantitative projects, outline the relevant Power calculations and the rationale for assuming given effect sizes. For qualitative projects, outline your reasoning for assuming that this sample size will be sufficient to address the study's aims
IRAS A59 and IRAS A60

As there is limited research in this area, multiple methods were employed to estimate the sample size required for sufficient power. G*Power, an online power analysis program for statistical tests was utilised initially (Faul et al., 2009). In order to test the principle research question, an a priori analysis using a linear multiple regression fixed model with a single regression co-efficient was input. A two tailed approach with a medium effect size ($f^2 = 0.15$) and alpha level of 0.05 indicated that for 7 predictor variables, a sample size of 89 would be required.

A commonly used "rule of thumb" was also used to estimate sufficient power. Researchers have recommended a 10:1 ratio of cases to predictors (Peduzzi et al., 1996). In this study there are the 7 predictor variables of interest, indicating that 70 participants are needed. However, these recommendations vary, and Green (1991) suggests a minimum sample size of 104 is needed plus the numbers of predictors (7), which would equate to 111 (VanVoorhis et al., 2007). Additionally, similar studies which have investigated the prevalence of alcohol use in pregnant women have had larger sample sizes. For example, Smith et al (2014) recruited 409 women from antenatal clinics in the South West of England using an anonymous questionnaire. Participants were given hard copies of the questionnaire to compete and return via an envelope in the post.

For analyses of secondary research questions, independent sample t tests will be conducted. G*Power analysis indicates that in order to achieve statistical power, with a two tailed approach, an alpha level 0.05 and large effect size of .5, a sample size of 210 is required. This equates to 105 women who were pregnant before April 1st 2016, and 105 women who have been pregnant after this date.

Recruitment will take place across multiple sites and platforms and so although approximately 200 participants are required for statistical analyses, the study hopes to recruit more than this. Studies which typically employ methodology similar to this study have had large numbers. For example, Nilsen et al. (2008) conducted a study assessing women's alcohol consumption during pregnancy through mailed anonymous questionnaires. They had a response rate of 61% and recruited a sample size of 869 women over the period of one year.

4.2 Outline reasons for your confidence in being able to achieve a sample of at least this size
E.g. give details of size of known available sample(s), percentage of this type of sample that typically participate in such studies, opinions of relevant individuals working in that area

According to National Statistics, the birth rate in Scotland has remained at approximately 54,000 per year over the past few years (Scottish Government, 2017). Maternity services exist across all 14 NHS Boards, as well as local third sector organisations such as Maternal Mental Health Scotland, Homestart, National Childbirth Trust & Netmums. In the trainee's health board there is one maternity unit in the catchment area which recorded 3350 live births from April 2016-2017. High rates of pregnancy in the health board and across Scotland will allow the study to recruit from multiple settings such as GP clinical waiting areas and third sector organisations. Leaflets for the study will be distributed amongst these as well as in the 2 antenatal centres in the health board.

Online survey research has many advantages including better access to participants that are usually difficult to reach, as well as being time efficient and cost-effective. It enables the trainee to overcome some of the barriers associated with in-person recruitment, particularly due to the sensitive nature of this study. By anonymising the data it is hoped that individuals feels comfortable to report more transparently their level of alcohol use and perceptions of current screening measures. Additionally, the use of Internet broadens the range of potential participants. Scottish health survey indicated that 83.4% of adults in Scotland used the internet for personal use in 2016, with 65% using it for social media purposes (Scottish Government, 2017). Studies have found that social media platforms such as Facebook have recruited samples representative of the population (Nelson et al., 2014) and have enabled recruitment in difficult to reach populations (Ramo & Prochaska, 2012). Furthermore, Ibarra et al. (2018) conducted a study examining the feasibility of using online platforms to recruit a difficult to reach population, women who smoke during pregnancy. Findings revealed that the Qualtrics platform had a recruitment rate of 84%, illustrating its efficiency in studies similar to the one proposed here.

These methods of recruitment hope to provide a wide access to large numbers of potential participants and the sample size is expected to be larger than the size required for statistical power. Furthermore, the study has proposed a recruitment time of 10 months. Other services which can be targeted outside of the Health board are online platforms such as Mumsnet, Facebook, twitter, and organisations such as Alcohol Focus Scotland, Scottish Drug Forum, Addaction and Phoenix Futures. It is hoped that by targeting services for individuals with drug and alcohol use difficulties there will be more of a diverse sample of participants with differing levels of alcohol consumption during pregnancy.

Section 5: Analysis

5.1 Describe the methods of analysis (statistical or other appropriate methods, e.g. for qualitative methods) by which the data will be evaluated to meet the study objectives
IRAS A62

Responses will be recorded using the Qualtrics survey platform, and subsequently the data will be transferred to IBM SPSS 24 for coding and analysis. The study intends to conduct statistical modelling techniqes such as regression analysis to investigate the relationship between independent variables such as the demographic factors, on the dependent variable, level of alcohol use during pregnancy. In order to answer the primary research question, analyses will explore the relationship between socio-economic status and level of reported alcohol use, as well as other factors which predict higher levels of alcohol use. Multiple linear regression analyses will be conducted to make predictions and identify significant relationships between the dependent variable and independent variables. This will be on the basis that the data meets numerous assumptions including a linear relationship between independent and dependent variables, little or no multicollinearity, homoscedasticity, multivariate normality and no auto-correlation (Osborne et al., 2002).

Independent sample t tests will be conducted to answer secondary research questions. This will compare the means of reported alcohol use in females who were pregnant before and after

guidelines on recommended alcohol use during pregnancy had changed (pre and post April 1st 2016).

Analysis of participants' attitudes to current alcohol screening instruments will be investigated using Likert scales. Analysis will be more of an exploratory approach rather than hypothesis testing and will be used to guide interpretation of results. Data on each of the scales will be coded from 1 (least comfortable) to 5 (most comfortable). A descriptive analysis will be completed for these as well as for a free text box which will be added at the end of the survey. This text box will allow participants to comment on their thoughts about the survey as a whole. Depending on the uptake and content of this, the trainee may analyse this information using a qualitative method; thematic analysis. This information will be used in the discussion section to further aid in the interpretation of results and make recommendation for future research.

Section 6: Project Management / Timetable

6.1 Outline a timetable for completion of key stages of the project

E.g. ethics submission, start and end of data collection, data analysis, completion of systematic review

Project Management Gannt Chart

Task	Year 1				Year 2						Year 3			
	May-Jun	Jul-Aug	Sep-Oct	Nov-Dec	Jan-Feb	Mar-Apr	May-Jun	Jul-Aug	Sep-Oct	Nov-Dec	Jan-Feb	May-Apr	May-Jun	Jul-Aug
Thesis proposal submission	X													
Ethics application preparation		X												
Ethics submission			X											
Study Preparation		X	X	X										
Systematic review				X	X	X	X	X	X					
Data collection					X	X	X	X	X					
Data analysis									X	X				
Thesis write up							X	X	X	X	X			
Submit draft to supervisor											X	X		
Final corrections												X		
Thesis submission													X	
Viva													X	
Dissemination														X

Section 7: Management of Risks to Project

7.1 Summarise the main potential risks to your study, the perceived likelihood of occurrence of these risks and any steps you will or have taken to reduce these risks. Outline how you will respond to identified risks if they should occur

Failure to receive ethical approval
This study may fail to receive ethical approval due to concerns raised regarding the possibility of adverse outcomes to individuals who partake in the study. As discussed in section 1, disclosure of alcohol use during pregnancy can result in the person feeling guilty or blamed. The perceived likelihood of this risk is low however, as there appears to be no research to suggest that asking questions on alcohol use during pregnancy causes significant harm, and alcohol screening instruments are used routinely in practice (Chang, 2001).

Participants will be directed to an information sheet before commencing the study and will be informed of the sensitive nature of the study. In the event that participants may become psychologically distressed, they will be directed at the beginning and end of the study to helplines and services they can access for support.

Issues with recruitment
Alike other studies, a major risk is that the study fails to recruit a sufficient number of participants and that the study may be underpowered. In order to mitigate the risks of this, recruitment will take place across several settings (as detailed in section 3.4). Third sector organisations and use of social media platforms should further reduce the possibility that the study will recruit insufficient numbers. Additionally, this study is predicted to have approximately 10 months for data collection, allowing for further organisations and services to be targeted across health boards if required.

Stigma associated with alcohol use is a further potential risk for lack of recruitment. Participants may not wish to disclose their level of alcohol use during pregnancy or may under-report this, which may result in a skewed participant pool. Furthermore, the study's sample will be self-selecting and so bias is likely.
Studies have shown that women are likely to underreport consumption or deny alcohol use out of embarrassment (Morrow-Tlucak et al, 1989). The study aims to mitigate this risk by anonymity, and participants are not obliged to disclose this information should they wish not to.

Studies utilising population surveys have indicated other factors associated with under-reporting, including memory difficulties due to high levels of alcohol consumption, the manner in which questions are constructed, and high non-participation rates in samples with high levels of use (Sobell & Sobell, 1995). In order to address some of these concerns, this study aims to construct objective questions and target populations where there is likely to be higher numbers of alcohol or substance use problems. Participants will be identified from these groups by answering an item asking how they had come across the study.

Length of battery
The study is estimated to take 15 minutes. All individuals will be directed to an information sheet and consent form upon signing up for the study, and a debriefing form at the end. It is possible that attrition will occur during the study as individual's choose not to complete all items. The study aims to recruit larger numbers than needed for a sufficient sample size to account for this possibility and reduce the impact of this on overall sample size analysis.

Data storage
All data will be entered via an online platform and will be stored anonymously and securely within the University of Edinburgh database (see Section 3.1). The perceived risks around data storage and loss of data is relatively low.

Section 8: Knowledge Exchange

8.1 How do you intend to report and disseminate the results of the study?
IRAS A51

The proposed study and its hypotheses will be pre-registered on the Open Science Framework before data collection and will be accessible online via the Open registries Network (https://osf.io/registries). This hopes to promote transparency and quality, improve the credibility of the research findings, and reduce 'hindsight bias' whereby data is used to generate a post-diction or explanation of results (Noseck et al., 2019). It will be written up in a portfolio format which will include a systematic review of the literature, and the results of the empirical research project conducted. It will be submitted as a Clinical Psychology Doctorate Thesis to the University of Edinburgh and subsequently uploaded to the Edinburgh Research Archives database which is freely accessible online.

It will be prepared for submission to an academic journal such as the UK Journal of Public Health which has an impact factor of 1.7. Other studies investigating PAU and healthcare professional attitudes have published in similar journals in order to target the most appropriate population (Payne et al., 2005) (Zicco & Racine, 2017). The trainee also plans to present the research at a departmental conference within their health board and seek opportunities at other relevant events such as local conferences, CPD events and poster sessions. As the Scottish Government has recommended further research to be conducted in this area, results will be cascaded to members of the committee who will be actively involved in the design of this research project, and further disseminated to health care professionals such as GP's and midwives in order to help inform practice.

In order to disseminate the study to a wider audience and the general population who may have participated in the study, this article will be shared on social media platforms such as Twitter, Linkedin and Facebook. A lay summary of the research will be posted on forums such as Mumsnet and Alcohol Focus Scotland with permission, to reach individuals who may not have participated in the study and further raise awareness of alcohol use during pregnancy.

8.2 What are the anticipated benefits or implications of the project?
E.g. if this is an NHS project, in what way(s) is the project intended to benefit the NHS?

This study aims to gain a more transparent perspective on the prevalence of alcohol consumption during pregnancy in Scotland. Existing prevalence data is under representative of the general population and does not correspond with alcohol sales (Scottish Health Survey, 2015) (Sharp et al., 2014). Despite increased awareness and acknowledgment of the risks associated with PAU, rates of consumption remain high at 41%. Guidelines for recommended PAU have changed, and there appears to be no research conducted on level of education surrounding this since. This study aims to address this gap in the literature, as well as exploring other factors associated with alcohol use during pregnancy, such as sociodemographic factors and history of mental health difficulties.

The Scottish Government has recently highlighted the need for further research in the area of PAU and FASD. SIGN guidelines recommend work in diagnoses and early intervention for FASD. As PAU is a direct cause of FAS and FASD, it is important to understand how information on alcohol consumption can be elicited in a more transparent, less stigmatised manner. This information is crucial in identifying children who have been prenatally exposed to alcohol, but which is not reported in their medical records.

This study has the potential to improve likelihood of diagnoses of FASD in this population by highlighting a more realistic prevalence of PAU in Scotland and exploring the most appropriate ways in which this can be assessed. At present there is minimal published research on factors relating to underreporting of alcohol consumption and this aims to add to the literature base in providing a better understanding of this. It hopes to inform recommendations for healthcare providers about how best to screen for alcohol consumption in pregnant women and better predict risks of FASD. This study also aims to indirectly improve patient's engagement with health

services and improve quality and transparency of care through recommendations made from the findings.

8.3 Are the any potential costs for the project?
Outline any potential financial costs to the project, including the justification for the costs (why are these necessary for the research project?) and how funding will be obtained for these costs (how will they be met?) Please separate these into potential costs for the University and potential costs for your NHS Board and note that you should ask your NHS Board to meet stationery, printing, postage and travel costs.

University of Edinburgh

There are no foreseen costs for the University of Edinburgh as measures are freely available, and the survey platform Qualtrics is funded by the University for use by students.

NHSXXX

Minimal costs are anticipated for the NHS health board. Leaflets for the study will be printed and distributed across several sites. This may incur some travel costs however this is expected to be minimal due to the geography of the health board and of centres located nearby the trainee's base. There will be some postage costs for the distribution of leaflets to third sector organisations. It is also anticipated that there will be printing costs for a research poster to be used as part of the study's dissemination. Funding for these materials will be applied for once ethical approval has been sought.

Section 9: Any Other Relevant Information

N/A

Section 10: Key References

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Section 11: Confirmation of Supervisors' Approval	
"I confirm that both my Academic and Clinical Supervisors have seen and approved this research proposal and have both completed the supervisors' appraisal forms below." *Delete as appropriate*	
Yes	No

Appendix 1

Main Academic Supervisor's Appraisal of Project Risk

Date
24/05/19

Do you consider that the project should proceed in broadly its current form? *Delete as appropriate*		
Yes		

Outline the reasons for the above response Highlight any areas of risk to the completion of the project that have not been fully addressed within the proposal and any steps that could be taken to reduce risks
I am pleased that Orlagh has chosen to pursue a study in what is an area of current concern for the Scottish Government and which addresses an importance healthcare issue. Despite significant efforts by Orlagh to identify a project that would include the neuropsychological assessment of affected children extensive consultation with her healthboard have indicated that this will not be possible. Instead Orlagh has devised this attached study as a means to make an important contribution to this area in the absence of such assessments. I believe that the study is feasible and would value the opinion of the marker on whether they consider it sufficient to meet the requirements of the D.Clin.Psych.

Appendix 2

Clinical Thesis Supervisor's Appraisal of Project Risk

Date
28/05/2019

Do you consider that the project should proceed in broadly its current form? *Delete as appropriate*		
Yes		

Outline the reasons for the above response Highlight any areas of risk to the completion of the project that have not been fully addressed within the proposal and any steps that could be taken to reduce risks

I think the online nature of the questionnaire means we would be successful in recruitment, and the ability to skip questions or drop out will ensure participants feel comfortable in answering as required, as well as giving us valuable information about the questions used in clinical practice. The debriefing sheet will ensure participants are directed to suitable support should the questionnaire trigger concerns relating to their own or their children's well-being.

Appendix D: Participant Information Sheet

Research study: Pregnancy, Alcohol and Behaviour: The impact of an information leaflet on women's attitudes towards drinking during pregnancy

Thank you for following the link to this study. We are very pleased to invite you to take part. Please read this Participant Information Page before you decided whether or not you wish to take part.

What is the purpose of the study?
As part of an education programme this study explores women's knowledge, use and attitudes towards drinking during pregnancy. We want to find out if these factors influence how much women drink while they are pregnant. We are also interested in the effect of an information leaflet on women's attitudes. We hope that by better understanding alcohol use during pregnancy we will be able to provide better support for women during their pregnancy.

Who can take part?

Women who are:

- at least 18 years old;
- currently, or have been pregnant at any point since April 1st 2016
- able to read and write to a secondary school level.

Those who are below the age of 18, who have not been pregnant since April 2016, or those whom have additional support needs will be excluded from taking part in the study.

What will the survey ask?

- It will direct you first to a consent page where you will be asked to provide your consent should you wish to participate in the study
- The survey will then ask: some information about yourself e.g. age, ethnicity, marital status, level of education, employment status and general questions about your most recent pregnancy.
- Some general questions about your behaviour e.g. how you react when good things happen to you
- Your alcohol use before and after you found out that you were pregnant
- Your beliefs and attitudes towards drinking during pregnancy

We'll then ask you to read an information leaflet on drinking in pregnancy before asking you a small number of questions to measure if the leaflet has changed your attitudes. Completing the survey will take approximately 20 minutes.

Do I have to take part? No, it's up to you whether you would like to take part. Participation is voluntary and you can withdraw at any time, without giving a reason and without adverse consequences or academic penalty, by closing the browser window. As your participation is anonymous, it will not be possible to remove your data. Once you start the survey you will have 1 week to complete it. If you do not complete it within this time the survey will automatically close and your data will be recorded as a partial response.

Are there any benefits? This study hopes to reduce the stigma associated with alcohol use during pregnancy by providing a safe and anonymous space to share your views. In addition to the opportunity to enter our prize draw, your answers will help us better understand alcohol use during pregnancy and whether an information leaflet has a positive impact.

As a thank you for your time, at the end of survey you will have the chance to enter a prize draw for a chance to win one of three £50 Amazon gift cards. This will direct you towards an anonymous link where you can enter an email address to take part.

Are there any disadvantages?
There are no known risks for you in this study. However, we are aware that the topic of pregnancy and alcohol can be regarded as sensitive. We don't think that our questions will cause any discomfort but, we've provided details of support services at the end of the study on the debrief form and on our web-page. Please take some time to read the information about where to seek appropriate support should you feel distressed and remember that you can also exit the survey at any time by exiting the browser.

Will my taking part in the study be kept confidential? YES. All of the information collected from the survey will be kept confidential and processed in accordance with the Data Protection Law. The survey software does not collect information that would allow us to identify any information about you. All information collected will be stored in a single secure data centre which complies with UK standards.

If you choose to enter into the prize draw on completion of the study, you will be directed to a separate link in order to provide an email address. This email address will be stored separately to your responses to the survey in order to ensure that your anonymity is preserved and will be deleted once the prize draw has been completed in June 2021.

What will happen to my data?
The research data collected during the study may be looked at by project researchers from the University of Edinburgh. The University of Edinburgh is the sponsor for this study based in the United Kingdom. We will be using information from you in order to undertake this study and will act as the data controller for this study. This means that we are responsible for looking after your information and using it properly. The University of Edinburgh will keep anonymised information about you for a minimum of 5 years after the study has finished. For general information about how we use your data go to: https://www.ed.ac.uk/records-management/privacy-notice-research

What will happen when the study is finished? Once the study is completed, the researcher will prepare a report which will summarise the findings of the study. You will not be identifiable in any report or publication. This report may be published in a scientific journal and/or disseminated to the wider research community. Your anonymised data will be stored for a minimum of 5 years and may also be used in future ethically-approved studies. You will be able to access a summary of the study's results on our webpage once completed. Please check the following webpage from July 2021 onwards: (please see link to webpage below).

Who is organising and funding the research? The study has been sponsored by the University of Edinburgh and funded by NHS Education Scotland as part of their support for the East of Scotland Clinical Psychology Doctoral Training Programme.

Who has reviewed the study?
This project has been approved by the Ethics Review Committee at School of Health in Social Science at the University of Edinburgh.

If you would like further information, please contact the Chief Investigator: Orlagh Keating at pregnancy.behaviour@ed.ac.uk

If you wish to discuss the study further with the project's academic supervisor, please contact:
Dr Suzanne O'Rourke, University of Edinburgh at Suzanne.O'Rourke@ed.ac.uk

If you would like to discuss the project with someone independent of the study, please contact:
Dr. Angus MacBeth, University of Edinburgh at angus.macbeth@ed.ac.uk

If you would like to make a complaint about the study, please contact: The University of Edinburgh Research Governance Team at cahss.res.ethics@ed.ac.uk

If reading this has raised any questions or made you feel uncomfortable in any way, you can find support from the following services:

- Your GP
- Your Midwife or Health Visitor
- NHS 24 (dial 111)
- Samaritans – confidential listening service (dial 116 123)
- Breathing Space – confidential listening and signposting to other services (dial 0800 838 587)
- Maternal Mental Health Scotland – for information and signposting to helpful services (maternalmentalhealthscotland.org.uk)
- Drinkline - National confidential helpline for anyone who is concerned about their drinking, or someone else's, dial 0300 123 1110, weekdays 9 am to 8 pm, weekends 11 am to 4 pm

Self-care tips:
You may also want to try the following acts of self-care to help yourself feel more settled:

- Take time out to quietly enjoy a warm drink;
- Go for a gentle walk;
- Take a bath;
- Speak to a friend who makes you feel understood.

You can also visit the study's webpage here:
https://v3.pebblepad.co.uk/spa/#/public/w4WgzHRyM9b3HxZmfn8tjrqHyM

Appendix E: Consent form

THE UNIVERSITY of EDINBURGH

Participant Consent Page (Administered via Qualtrics)

Title of Study: Pregnancy, Alcohol and Behaviour: The impact of an information leaflet on women's attitudes towards drinking during pregnancy

Clicking on the "agree" button below indicates that you give your consent to the following:

1. I confirm that I have read and understand the information sheet (version 2 dated 08 July2020) for the above study. I have had the opportunity to consider the information, ask questions and have had these answered satisfactorily.
2. I am participating voluntarily and understand that I am free to withdraw from the study at any time, without giving any reason, and without adverse consequences or academic penalty.
3. I understand that the research data collected during the study may be looked at by project researchers from the University of Edinburgh. I agree to give permission for these individuals to access my data.
4. I agree to give permission for my anonymised responses to the survey to be used in the researcher's publications on this topic.
5. I understand that if I wish to enter the prize draw I will be asked to provide an email address which will be kept until the winners of the draw have been chosen at the end of the study (June 2021). I understand that this email address will not be linked to my survey responses.
6. I understand that relevant sections of my data collected during the study may be looked at by individuals from the Sponsor (University of Edinburgh), where it is relevant to my taking part in this research. I give permission for these individuals to have access to my data.
7. I understand that my anonymised data collected will be retained for a duration of 5 years following completion of the study and may be used in future ethically approved research.
8. I agree to the above consent points and agree to participate in the above research study.

If you do not wish to participate, please decline participation by clicking on the "disagree" button or exit the survey by closing your browser.

Agree ☐

Disagree ☐

Appendix F: Poster

Appendix G: Information Leaflet

Retrieved from https://www.rcog.org.uk/globalassets/documents/patients/patient-information-leaflets/pregnancy/pi-alcohol-and-pregnancy.pdf

Health & care information you can trust

Royal College of Obstetricians & Gynaecologists

Information for you

Published in February 2015 (Reviewed in January 2018)

Alcohol and pregnancy

About this information

This information is for you if you are pregnant or are planning to have a baby. It outlines the effects of drinking alcohol on your baby's development in the uterus (womb). It may also be helpful if you are a partner, relative or friend of someone who is pregnant or planning a pregnancy and want to know more about the effects of drinking alcohol during pregnancy or while planning to have a baby.

A glossary of all medical terms is available on the RCOG website at: www.rcog.org.uk/en/patients/medical-terms.

Key points

- The safest approach is not to drink alcohol at all if you are pregnant, if you think you could become pregnant or if you are breastfeeding.
- Although the risk of harm to the baby is low with small amounts of alcohol before becoming aware of the pregnancy, there is no 'safe' level of alcohol to drink when you are pregnant.
- Drinking alcohol during pregnancy can affect the way your baby develops and grows in the uterus (womb), your baby's health at birth, and your child's long-term health.
- Drinking heavily throughout pregnancy can result in your baby having severe physical and mental disability known as fetal alcohol syndrome (FAS).
- It is important that you tell your healthcare professional(s) about your drinking so that appropriate support and information can be offered to you.

How will drinking alcohol affect my unborn baby?

Avoiding alcohol during pregnancy is the safest option. There is no proven safe amount of alcohol a woman can drink during pregnancy.

If you drink alcohol during pregnancy, some alcohol will pass through the placenta to your baby. The more you drink the greater is the risk of harm to your baby.

Drinking heavily during pregnancy can:

- increase your chances of miscarriage
- affect the way your baby develops in the uterus and, in particular, the way your baby's brain develops
- affect the way your baby grows in the uterus by causing the placenta not to work as well as it should – this is known as fetal growth restriction (for more information, see the RCOG patient information *Having a small baby*, which is available online at: www.rcog.org.uk/en/patients/patient-leaflets/having-a-small-baby)
- increase the risk of a stillbirth
- increase the risk of premature labour
- make your baby more prone to illness in infancy and in childhood, and also as an adult
- cause fetal alcohol spectrum disorder (FASD) or fetal alcohol syndrome (FAS) – see below for more information on both FASD and FAS.

The more you drink, the more your baby's growth will be affected and the less healthy your baby will be. However, if you cut down or stop drinking altogether, your baby will start to grow at a normal rate. Stopping drinking at any point during pregnancy can be beneficial. However, in some instances, the effects of heavy drinking on your baby cannot be reversed.

What are fetal alcohol spectrum disorder (FASD) and fetal alcohol syndrome (FAS)?

Drinking heavily during pregnancy can cause fetal alcohol spectrum disorder (FASD) or fetal alcohol syndrome (FAS).

While FASD is less severe than FAS, children with FASD can have learning difficulties, problems with behaviour, physical disability, and emotional and psychiatric problems that last a lifetime. Whether or not a baby is affected mildly or severely with FASD is directly linked to how much and how often a woman drinks during pregnancy.

Heavy drinking of alcohol or drinking alcohol regularly in pregnancy is harmful for babies and may result in a serious condition called fetal alcohol syndrome (FAS). Children with FAS usually have severe physical and mental disability. For more information, see the resources available from NOFAS (National Organisation for Foetal Alcohol Syndrome-UK) at: www.nofas-uk.org.

What if I am thinking of having a baby?

If you are planning a pregnancy, it is advisable not to drink alcohol during this time. Either partner drinking heavily while trying to become pregnant, can make it more difficult to conceive.

I have just discovered I am pregnant and I have been drinking. What does this mean for my baby?

Most babies will be fine. Talk to your midwife or doctor who will be able to advise you.

Will I be asked how much alcohol I drink when I am pregnant?

At your antenatal appointment, your midwife will ask you about your medical history and your lifestyle. This will include talking about your alcohol intake, if any.

Your midwife will offer you information and support on how to cut down or stop drinking alcohol.

Can I drink alcohol if I want to breastfeed?

The safest option is to avoid alcohol during breastfeeding as alcohol can find its way into your breast milk. Regular drinking during breastfeeding may affect your baby's development.

If you do choose to drink, it is safest not to drink more than 14 units per week and best to spread your drinks evenly during the week.

Support for you

There are a number of reasons why women might drink too much alcohol while they are pregnant:

- they might not know they are pregnant
- they might feel under pressure to drink when with friends
- they might be trying to cope with problems and stress
- they might not be aware of the risks of drinking alcohol during pregnancy.

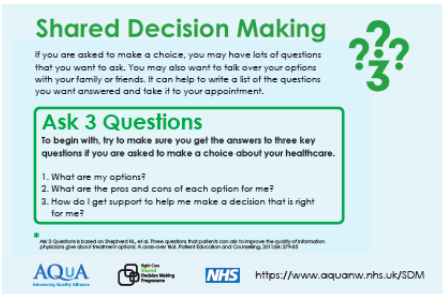
If you would like to talk to someone about your drinking, you can speak to your midwife, obstetrician, practice nurse, GP or health visitor. Once they know how you are feeling and why you are drinking, the person you tell will be in a better position to offer you the right help and information.

It may be helpful to think about the questions below:

- How much and how often have you been drinking?
- Are you unable to remember what happened on an occasion when you were drinking?
- Has your behaviour changed because of your drinking?
- Has a relative, friend, work colleague, doctor or health worker expressed concern about your drinking?

You will be supported directly or given advice about where to find local counselling or support services available to you. See the *Further information* section below.

Making a choice



Further information

UK Chief Medical Officers' Low Risk Drinking Guidelines (Department of Health, 2016), which is available at: www.gov.uk/government/publications/alcohol-consumption-advice-on-low-risk-drinking

Drinkline is the national alcohol helpline: if you're worried about your own or someone else's drinking, you can call this free helpline, in complete confidence; call 0300 123 1110 (weekdays 9 am to 8 pm, or weekends 11 am to 4 pm)

NOFAS-UK (National Organisation for Foetal Alcohol Syndrome-UK): www.nofas-uk.org

The FASD Trust: www.fasdtrust.co.uk

Sources and acknowledgements

This information has been developed by the RCOG Patient Information Committee. It is based on the *UK Chief Medical Officers' Low Risk Drinking Guidelines* (Department of Health, 2016), which is available at: www.gov.uk/government/publications/alcohol-consumption-advice-on-low-risk-drinking.

This leaflet was reviewed before publication by the RCOG Women's Network and by the RCOG Women's Voices Involvement Panel.

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